35th Annual

In-Training Examination for Radiation Oncology Residents

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1. Which is a risk factor for renal medullary cancer?
   a. Von Hippel-Lindau (VHL) disease
   b. Sickle cell Trait
   c. Tuberous Sclerosis
   d. Kidney Stones

   **Key:** B
   **Rationale:** Renal medullary carcinoma is a highly aggressive malignancy often found in young, black patients with sickle cell trait.
   **References:** Swartz MA, Karth J, Schneider DT, Rodriguez R, Beckwith JB, Perlman EJ. Renal medullary carcinoma: clinical, pathologic, immunohistochemical, and genetic analysis with pathogenetic implications. Urology, 2002 Dec; 60(6), 1083-1089.

2. Based on ICRU-83, the Treated Volume (TV) can be best defined as the:
   a. V5%
   b. V20%
   c. V50%
   d. V98%

   **Key:** D
   **Rationale:** ICRU 83 suggests that the treated volume—e.g. volume of tissue receiving a “therapeutic dose” of radiation—might be defined by V98%.
   **References:** Dieterich S et al. Practical Radiation Oncology Physics. Elsevier. 2016. 1st Ed.

3. An electron scattering foil is used in a LINAC to scatter the beam across the treatment field. What is the approximate relative dose in the beam due to x-ray contamination from the foil?
   a. 5%
   b. 10%
   c. 15%
   d. 20%

   **Key:** A
   **Rationale:** In a modern linac, typical x-ray contamination dose ranges up to 5% for beams up to 20MeV.

4. In addition to abdominal ultrasound, what imaging studies are routinely required for staging a newly diagnosed Stage III Wilms tumor with favorable histology?
   a. MRI brain, bone scan
   b. Chest CT, bone scan
   c. Chest CT, MRI brain
   d. Chest CT only

   **Key:** D
   **Rationale:** Abdominal ultrasound is preferred at diagnosis for its ability to provide vascular invasion and flow information about the renal vessels as well as delineate the primary tumor extent with non-irradiative means. Chest CT is preferred at diagnosis to delineate any findings concerning for metastatic disease. Given the radiation exposure related to use of CT, many providers will switch to chest x-rays following the initial evaluation. An MRI of the brain is only required for clear cell sarcoma of the kidney, malignant rhabdoid tumors and renal cell carcinoma while bone scans are typically only required for clear cell sarcoma and renal cell carcinoma.
   **References:** John A Kalapurakal THE LANCET Oncology; AREN0321; Vol 5 January 2004; 37-46.
5. In the ACOSOG Z6041, patients with cT2N0 rectal adenocarcinoma were treated with preoperative chemoradiation followed by local excision. What was the approximate 3-year DFS?
   a. 60%
   b. 70%
   c. 80%
   d. 90%

Key: D
Rationale: Patients with clinical T2N0 rectal adenocarcinoma staged by endorectal ultrasound or endorectal coil MRI, measuring less than 4 cm in greatest diameter, involving less than 40% of the circumference of the rectum, located within 8 cm of the anal verge were included in the study. Neoadjuvant chemoradiotherapy consisted of capecitabine (original dose 825 mg/m2 twice daily on days 1-14 and 22-35), oxaliplatin (50 mg/m2 on weeks 1, 2, 4, and 5), and radiation (5 days a week at 1.8 Gy per day for 5 weeks to a dose of 45 Gy, followed by a boost of 9 Gy, for a total dose of 54 Gy) followed by local excision. Because of adverse events during chemoradiotherapy, the dose of capecitabine was reduced to 725 mg/m2 twice daily, 5 days per week, for 5 weeks, and the boost of radiation was reduced to 5.4 Gy, for a total dose of 50.4 Gy. The estimated 3-year disease-free survival for the intention-to-treat group was 88.2% (95% CI 81.3-95.8), and for the per-protocol group was 86.9% (79.3-95.3).


6. In Indelicato et al., Acta Oncologica (2014), what was the rate of symptomatic brainstem toxicity among pediatric brain tumor patients treated with proton therapy who received a maximum brainstem dose > 56.5 Gy?
   a. 2%
   b. 5%
   c. 10%
   d. 25%

Key: C
Rationale: Answer: B. Although the overall incidence of symptomatic brainstem injury was 3% among the patients treated with proton therapy, subset analysis showed the rate of symptomatic brainstem injury among patients who had tumors of the posterior fossa, had a maximum point dose of D50% > 52.3 Gy, or maximum point dose > 56.5 Gy was approximately 10%.


7. For low LET irradiation with a high oxygen enhancement ratio (OER) in regions of the tumor, tumor cell killing is:
   a. lowest when the tumor cells are well-aerated
   b. greatest in hypoxic conditions
   c. greatly reduced at 5% oxygen versus 20% oxygen
   d. greatly reduced at 0.5% versus 20% oxygen

Key: D
Rationale: Radiation with a high OER, such as X-rays, exhibit enhanced cell kill under aerated conditions and reduced within hypoxic regions. The radiation sensitivity of cells is reduced as the partial pressure of oxygen drops below ~30mm Hg (~5% oxygen). The OER is greatest below this point. Partial pressure of oxygen at ~ 3mm Hg approximates the radiosensitivity halfway between a hypoxic and aerated condition. Thus, cell kill is dependent on oxygen concentration, and will be decreased at partial pressures below 30 mm Hg, certainly at 3 mm Hg. Little increase in radiation sensitivity is seen at partial pressures greater than 30 mm Hg.

8. Involvement of which blood vessel would render a pancreatic mass borderline resectable?\ 
a. 180 degree involvement of the splenic artery, with splenic vein thrombosis 
b. 90 degree involvement of the celiac axis 
c. Obliteration of the portosplenic confluence 
d. 270 degree involvement of the superior mesenteric artery 

**Key:** B 
**Rationale:** A borderline resectable lesion is defined as one in which there is a higher likelihood of an incomplete surgical resection. As such, these patients are not good candidates for upfront resection in comparison to patients with resectable lesions. Answer A describes a resectable tumor, as the spleen and its vasculature are resected in a distal pancreatectomy. Answer C is resectable, as contact with the superior mesenteric vein must be >180 degrees in order to confer higher risk of positive margins and qualify as borderline resectable. Answer D involves >180 degrees of the superior mesenteric artery and is unresectable (also known as locally advanced). This patient would not be expected to be resected with negative margins without a response to pre-operative therapy. Answer B is borderline resectable, due to <180 degree involvement of the celiac axis. 

9. In the recent OnCoRe registry study of non-operative management for rectal cancer, what was the approximate rate of local tumor regrowth? 
a. 15% 
b. 25% 
c. 35% 
d. 45% 

**Key:** C 
**Rationale:** In this recent multicenter-registry study from the UK, the authors reported no difference in non-regrowth DFS or OS between surgical resection versus non-operative approach. However, 34% of patients in the non-operative group experienced local regrowth. Of these, 88% were surgically salvaged, emphasizing the need for close post-treatment surveillance with this approach. 

10. For mycosis fungoides, the palm plus the digits on one hand represent what percent of body surface area? 
a. 1% 
b. 3% 
c. 5% 
d. 10% 

**Key:** A 
**Rationale:** The palm and the digits of one hand represent 1% of total body surface area involved, when trying to assess how much of a patient’s skin is involved with mycosis fungoides. 
11. What is the limitation of the linear-quadratic ($\alpha/\beta$) cell survival model at high levels of cell kill?
   a. Under predicts survival at low doses
   b. Over predicts survival at low doses
   c. Under predicts survival at high doses
   d. Over predicts survival at the high doses

**Key:** C

**Rationale:** At low doses, the linear-quadratic $\alpha/\beta$ model does a good job at predicting cell survival. At higher doses while the model will predict a continuous bending of the survival curve, in reality, the curve “straightens” out; i.e. it becomes essentially exponential. This makes the model very useful for predicting outcomes for fractionated treatment regimens where a relatively large number of low dose fractions are used. When one or a small number of high dose fractions are delivered, the $\alpha/\beta$ model would tend to under predict survival under conditions similar to SBRT (at high levels of cell kill). Whether this under prediction is sufficiently large to affect treatment outcomes is under debate.


12. A glioma has IDH mutation, p53 mutation, ATRX loss, 1p deletion, and 19q intact. How should this tumor be classified according to the 2016 WHO classification?
   a. Medulloblastoma
   b. Astrocytoma
   c. Oligodendroglioma
   d. Pilocytic astrocytoma

**Key:** B

**Rationale:** In the 2016 WHO Classification of Brain Tumors, some of the molecular characteristics of an astrocytoma are: IDH mutation, p53 mutation, ATRX mutation leading to loss, and lack of co-deletion of 1p19q. A single deletion in 1p or 19q is not sufficient to make an oligodendroglioma diagnosis; they must be co-deleted. Furthermore, p53 mutation and ATRX loss together denote an astrocytoma and are largely mutually exclusive from 1p19q co-deletion.


13. What mean dose to the pharyngeal constrictors results in a 20% risk of dysphagia and aspiration?
   a. 40 Gy
   b. 50 Gy
   c. 60 Gy
   d. 70 Gy

**Key:** B

**Rationale:** 50 Gy mean dose to the constrictors results in a 20% risk of dysphagia and aspiration.

14. For cT1N0M0 breast cancer treated with breast-conserving surgery and sentinel lymph node biopsy with 1 of 2 sentinel lymph nodes positive without ECE {pT1cN1a(sn)}, which subsequent locoregional treatment option is best supported by level 1 evidence?
   a. Completion axillary dissection followed by whole breast radiation
   b. Completion axillary dissection followed by radiation of the breast and dissected axilla
   c. No further axillary surgery and whole breast radiation in the prone position
   d. No further axillary surgery and whole breast radiation +/- draining lymphatics

Key:  D

Rationale: The ACOSOG Z-11 trial enrolled women with T1-T2 clinically node negative breast cancer who underwent breast conserving surgery and SLNBx with 1 or 2 positive nodes. They were randomly assigned to axillary dissection or no further surgery. All patients subsequently received whole breast RT in the supine position, likely encompassing the low axilla in the tangent fields. Axillary dissection increased morbidity (notably lymphedema risk) without improving any oncologic endpoint. The EORTC AMAROS trial enrolled a similar population and randomized them to axillary dissection vs. radiotherapy to the axilla and SCV nodes. The two treatments yielded equivalent rates of regional recurrence and disease-free survival, but the RT arm was superior with regard to lymphedema rates. Therefore, axillary dissection should be omitted for women receiving RT. Also, results from the MA-20 and EORTC 22922 suggest that the addition of regional nodal irradiation in the setting of node-positive breast cancer improved disease-free survival and reduces breast cancer death and should therefore be strongly considered.


15. Regarding role of extrapleural pneumonectomy (EPP) in patients with mesothelioma:
   a. localized sarcomatoid mesothelioma should best be managed with EPP, chemotherapy and adjuvant RT
   b. pleurectomy/decortication followed by pleural based IMRT to 45 Gy in 25 fractions has similar outcomes than EPP followed by adjuvant RT
   c. post-operative radiation dose after EPP with negative margins is 60 Gy
   d. positive cytology for malignant cells in the pleural fluid is a contraindication for EPP

Key:  B

Rationale: A. Sarcomatoid mesothelioma has very poor prognosis and per NCCN is considered a relative contraindication for surgery. Chemotherapy is the appropriate option for these patients, and palliative radiation as indicated.
B. Per single institutional experience from MSKCC and a multicentre phase II study that used pleural based IMRT following pleurectomy/decortication for localized mesothelioma is an appropriate and safe option for therapy. Results appear promising and may be safer and more effective than historical data with EPP followed by adjuvant radiation.
C. Typical adjuvant RT dose after EPP with negative margins is 50-54 Gy, while with positive margins is 54-60 Gy.
D. Patients with localized mesothelioma often presents with pleural effusion. Patients with malignant cells in the pleural fluid is not considered metastatic and should be appropriately managed.

16. Which systemic therapy in combination with doxorubicin has been shown to improve PFS and OS in patients with advanced or metastatic soft tissue sarcoma?
   a. Dasatinib
   b. Eribulin
   c. Pazopanib
   d. Olaratumab

Key: D
Rationale: In a study of olaratumab and doxorubicin versus doxorubicin for soft tissue sarcoma, the combination showed improvement in overall survival (26.5 vs 14.7 mos) and progressive-free survival (6.6 vs 4.1 mos) compared to doxorubicin alone.

17. Which is accurate regarding different definitive treatment modalities for Stage I seminoma?
   a. There is a significant difference in RFS between treatment with chemotherapy and radiation therapy
   b. 3-year RFS after radiation is approximately 90%
   c. At least two cycles of chemotherapy are necessary to achieve the same disease control as 20-30 Gy of radiation
   d. Chemotherapy results in a greater proportion of para-aortic nodal failures compared with radiation

Key: D
Rationale: In stage I seminoma, whether randomized to one cycle of carboplatin chemotherapy or radiation, 5 year recurrence free survival was very good (95% vs 96%). Patients receiving chemotherapy experienced a higher rate of para-aortic nodal failures (74% vs 9%) while patients receiving radiation had a higher rate of pelvic failures (28% vs 0%).

18. As per the ABS guidelines, the equivalent dose (EQD2) in patients who have not responded well with a residual tumor greater than 4 cm at the time of brachytherapy is?
   a. <80 Gy
   b. 80 to 84 Gy
   c. 85 to 90 Gy
   d. >90 Gy

Key: C
Rationale: The EQD2 is 85-90 Gy in order to maximize local control in tumors greater than 4 cm at the time of implant. The toxicity associated with doses greater than 90 Gy would simply be too high. Doses lower than 80 greater would be inadequate. EQD2 between 80 to 84 are more appropriate for tumors that are less than 4 cm.
19. Per the RTOG 3-arm randomized trial (91-11), which treatment yielded optimal locoregional control for advanced laryngeal cancer?
   a. Induction chemotherapy followed by chemoRT to 70 Gy in 35 fractions.
   b. ChemoRT to 70 Gy in 35 fractions.
   c. Hyperfractionated radiation to 76.8 Gy in 64 fractions.
   d. Conventionally fractionated radiation to 70 Gy in 35 fractions.

Key: B
Rationale: The updated results of RTOG 91-11 continue to demonstrate superior locoregional control for eligible patients treated with chemoradiation, albeit without survival difference amongst the three tested arms (IC->RT, ChRT, and RT alone). Appropriate patient selection is key (as in this case, T3N0 disease, good baseline larynx function).

20. For a patient with histologic findings of neoplastic thymic epithelial cells with spindle shape, with great vessel invasion, what is the WHO Histologic Classification and Modified Masaoka stage?
   a. Type A, Stage IIB
   b. Type A, Stage IIIB
   c. Type B, Stage IIIA
   d. Type B, Stage IVA

Key: B
Rationale: Type A has neoplastic thymic epithelial cells with spindle/oval shape. Type AB has features of type A admixed with foci rich in lymphocytes. Type B1 resembles normal functional thymus, B2 has scattered plump cells with vesicular nuclei among a heavy population of lymphocytes, type B3 is predominantly composed of round or polygonal shape with minimal atypia, and type C is a thymic carcinoma with atypia with cytoarchitectural features no longer specific to the thymus. Modified Masaoka stage IIIA involves macroscopic invasion of neighboring organs such as pericardium, and lung without invasion of great vessels, whereas IIIB has invasion of great vessels.

21. What is a major safety risk of information technology systems in radiation oncology?
   a. Loss of data
   b. Failover protection
   c. DICOM transfers
   d. Auto File archiving

Key: A
Rationale: Failover protection and file archiving are used to mitigate impact if a system fails. DICOM transfers are standard actions and do not pose major safety risks.
22. Which soft tissue sarcoma subtype has a better DSS than other subtypes, but a higher local relapse rate?
   a. Angiosarcoma
   b. Leiomyosarcoma
   c. Malignant Peripheral Nerve Sheath Tumor
   d. Myxofibrosarcoma

**Key:** D

**Rationale:** In multiple institutional series, myxofibrosarcoma has demonstrated a better disease-specific survival than other sarcoma subtypes, but also a higher local relapse rate. Propensity for local recurrence is predicted by positive or close margins at resection. Aggressive surgery combined with radiotherapy may contribute to more effective local control.


23. A recent pooled analysis of two Phase-III studies (STARS and ROSEL) examining SABR/SBRT versus surgery for early stage NSCLC demonstrated:
   a. a statistically superior OS in favor of the radiation arm.
   b. a statistically reduced distant metastases in favor of the radiation arm.
   c. a statistically superior LRC in favor of the surgery arm.
   d. similar rates of grade 3-4 toxicity events in the two arms.

**Key:** A

**Rationale:** Estimated overall survival at 3 years was 95% in the SABR group compared with 79% in the surgery group (p=0.037). Recurrence-free survival at 3 years was 86% in the SABR group and 80% in the surgery group (p=0.54). Grade 3-4 toxicity rates were 44% in the surgery arm versus 10% in the SABR arm.

**References:** Chang JY. Lancet Oncology, 2015 Jun, 16(6):630-7.

24. What molecular marker provides prognostic information for grade II astrocytomas?
   a. INI-1
   b. WNT
   c. IDH
   d. Her2

**Key:** C

**Rationale:** Gliomas are classified by molecular status in view of data identifying molecular markers such as isocitrate dehydrogenase (IDH), to be predictive of clinical outcome. IDH mutation is associated with more favorable outcomes.


25. For the commissioning of a new LINAC, what is a 3D, scanning water tank system used to measure?
   a. Beam profiles
   b. Output versus gantry angle
   c. In-air output factors
   d. Head leakage

Key: A
Rationale: Option B is incorrect because the water tank would get in the way of measurements of output versus gantry angle. Option C is incorrect because in air measurements are taken without a water tank. Option D is incorrect because head leakage is measured in air and at the linac-specific location of highest leakage.

26. In an epidemiologic study, 500 workers with respiratory disease and 200 workers without respiratory disease were studied. Of those with disease, 250 reported exposure while only 50 without disease reported being exposed. This study is best described as a:
   a. case-control study.
   b. cohort study.
   c. cross-sectional study.
   d. randomized clinical trial.

Key: A
Rationale: A case-control study looks backward in time to detect a cause to a particular outcome. A cohort study occurs over extended time to study a characteristic suspected of being a precursor to the effect and tries to answer what will happen. A cross-sectional study is a snapshot of what is happening at the moment. A randomized clinical trial looks at the result relative to the intervention.

27. Regarding EORTC 22845, which randomized patients with low grade glioma to 54 Gy vs. observation, what outcome was improved by the use of early radiation therapy?
   a. Cognitive function
   b. Quality of life
   c. Progression free survival
   d. Overall survival

Key: C
Rationale: The EORTC 22845 trial randomized patients to 54 Gy vs observation. The median progression free survival was statistically different, 5.3 years vs 3.4 years and the 5 year PFS was 55% vs 35%. However the median overall survival was not statistically different at 7.4 years vs 7.2 years.
28. Which of the following isotopes is used for single photon emission computed tomography (SPECT)?
   a. $^{18}$F  
   b. $^{60}$Co  
   c. $^{82}$Rb  
   d. $^{99m}$Tc  

**Key:** D  
**Rationale:** $^{99m}$Tc is used in ~85% of nuclear medicine procedures. It satisfies many requirements for an injectable imaging radioisotope (emits a well-defined and highly detectable 140.5 keV gamma, has short physical and biological half-lives, can be produced with high specific activity, it is easy to use and store, etc.). $^{18}$F emits primarily positrons rather than photons, making it useful for positron emission tomography. $^{82}$Rb is also a positron emitter, albeit less common than $^{18}$F. $^{60}$Co is useful for teletherapy as it emits high energy gamma photons with a very long half-life, but as such is not suitable for injection or SPECT applications.  

29. What is the CNS classification for an asymptomatic child with ALL and 3 WBCs/µL in the CSF?  
   a. CNS 1  
   b. CNS 2  
   c. CNS 3  
   d. CNS 4  

**Key:** B  
**Rationale:** CNS involvement by ALL is described as:  
CNS 1: no blasts  
CNS 2: < 5 WBCs/uL with blasts  
CNS 3: >= 5 WBCs/uL with blasts, or the presence of a cranial nerve palsy  

30. What spinal cord dose results in a 50% risk of myelopathy?  
   a. 45 Gy  
   b. 55 Gy  
   c. 61 Gy  
   d. 69 Gy  

**Key:** D  
**Rationale:** 69 Gy has a 50% risk of myelopathy.  
31. The tumor PD-L1 expression enrollment requirement in the KEYNOTE-024 Phase-III randomized study for untreated advanced NSCLC (pembrolizumab vs chemotherapy) was:
   a. No requirement
   b. 1%.
   c. 5%.
   d. 50%.

   **Key:** D

   **Rationale:** To be eligible for the Keynote-010 study, patients with previously treated advanced NSCLC were required to have at least 1% tumor cells with PD-L1 expression. In the total patient population, median OS in the two pembrolizumab dose arms was significantly longer than docetaxel. In a planned subset analysis of patients with expression of PD-L1 on 50% of the tumor cells, median OS and PFS in the two pembrolizumab dose arms was significantly longer than docetaxel.


32. What site of localized Ewing Sarcoma is most likely to be treated with radiation alone?
   a. Left fibula
   b. Right 8th rib
   c. Right distal femur
   d. S1 vertebral body

   **Key:** D

   **Rationale:** In Ewing Sarcoma, the local therapy decisions are made by the radiation oncologist, surgeon, medical oncologist, and family based on feasibility and morbidity of surgery. “Expendable” or “dispensable” bones—such as the fibula, clavicle, ribs, or some bones of hand/feet—are very likely to be treated with surgery because the long-term morbidity of resection of these bones considered reasonable. Pelvic and sacral lesions, particularly those involving sacral nerve roots, are much more difficult surgeries and the surgeries can be very morbid.


33. In treating vulvar cancer with an involved pelvic lymph node, the superior field border can be raised what distance above the most cephalad-positive node?
   a. 2 cm
   b. 3 cm
   c. 4 cm
   d. 5 cm

   **Key:** D

   **Rationale:** The superior border should be no lower than the bottom of the sacroiliac joints or higher than L4/L5 junction unless the pelvic LNs are involved. If the pelvic LNs are involved the upper border can be raised to 5cm above the most cephalad-positive node.

   **References:** NCCN Vulvar Cancer; 1.2017
34. Receiver Operating Characteristic (ROC) curve is a plot of the true positive rate against the false positive rate for the different possible cut points of a diagnostic test. Which of ROC curve demonstrates the best test accuracy?

a. 

b. 

c. 

d. 
Key: C
Rationale: The area under the ROC is a measure of test accuracy. The closer the curve follows the left-hand border and then the top border of the ROC space, the more accurate the test. The closer the curve comes to the 45-degree diagonal of the ROC space, the less accurate the test.

35. In patients with Mycosis Fungoides who receive total skin electron beam therapy (TSEBT), a boost is required to which area?
   a. Elbows
   b. Hands
   c. Scalp
   d. Neck

Key: C
Rationale: The scalp, perineum, and soles of the feet require a boost because they involve body surfaces that are tangential to the TSEBT beam axis and therefore otherwise do not receive sufficient dose. The elbows, hands, and neck are adequately exposed and therefore do not require a boost.

36. Compared to patients who received temozolomide alone, what was the cognitive function and health-related QoL at 3 years for patients who received radiation alone on EORTC 22033-26033 for high risk, low grade glioma?
   a. Worse cognitive function, worse QoL
   b. Better cognitive function, worse QoL
   c. Better cognitive function, better QoL
   d. Similar cognitive function, similar QoL

Key: D
Rationale: The EORTC 22033-26033 study for high risk low grade gliomas randomized patients to either 50.4Gy versus temozolomide for up to 12 cycles. In their report of health-related quality of life and mini-mental status exam (MMSE), the analysis showed no significant differences between the groups for change in MMSE scores during 3 years of follow up for patients receiving radiation versus 1 year of temozolomide.

37. How did the addition of WBRT affect outcomes in the NCCTG N0574 randomized trial of SRS alone vs. SRS + WBRT for treatment of brain metastases?
   a. Improved OS, worse cognitive function
   b. Similar OS, worse cognitive function
   c. Improved OS, similar cognitive function
   d. Similar OS, similar cognitive function

Key: B
Rationale: Patients treated with SRS alone had less cognitive deterioration at 3 months compared to patients treated with SRS + WBRT. The median OS of patients treated with SRS + WBRT was 7.4 months vs. 10.4 months for SRS alone (HR, 1.02; 95% CI, 0.75-1.38; p = .92).
38. In patients with thymoma, the preferred choice of chemotherapy regimen for patients with unresectable disease is:
   a. carboplatin and paclitaxel
   b. cisplatin, doxorubicin and cyclophosphamide
   c. carboplatin and gemcitabine
   d. Bevacizumab, carboplatin and paclitaxel

**Key:** B  
**Rationale:** For locally advanced thymomas, induction chemotherapy with cisplatin, doxorubicin and cyclophosphamide (CAP) or CAP + prednisone is recommended with an overall response rate of 70% or more (Kim et al, Lung Cancer 2004). The alternate approach is induction chemoRT with CAP chemotherapy plus thoracic radiation therapy with a reported overall response rate of nearly 70% (Loehrer PJ Sr et al. JCO 1997). The preferred chemotherapy regimen for thymic carcinoma is carboplatin and paclitaxel. Other regimens are not recommended as first line therapy.  

39. Vaginal tumors are BEST visualized using MRI:
   a. T1 images.
   b. T2 images.
   c. T1 images with vaginal gel.
   d. T2 images with vaginal gel.

**Key:** D  
**Rationale:** Vaginal tumors generally are best seen on MRI using T2 images with vaginal gel inserted into the canal which distends the vaginal walls and aids in assessing the tumor’s thickness.  
**References:** ACR Appropriateness Criteria Management of Vaginal Cancer 2013.

40. According to GEC ESTRO recommendations for 3D image-based treatment planning for cervical cancer brachytherapy, which volume is used to assess high dose regions?
   a. V90
   b. V100
   c. V120
   d. V150

**Key:** D  
**Rationale:** Cumulative DVH are recommended for evaluation of complex dose heterogeneity. DVH parameters for GTV, HR CTV and IR CTV are the minimum dose delivered to the 90% and 100% of the respective volume: D90 and D100. The volume, which is enclosed by the 150% and 200% of the prescribed dose (V150 and V200) is recommended for overall assessment of high dose volumes.  
**References:** Jan, Potter, Recommendations from gynaecological (GYN) GEC ESTRO working group (II): concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy-3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology, 2006, Radiother Oncol, 78 (1), 67-77.
41. What describes beta-minus nuclear decay?
   a. A proton becomes a neutron, creating an electron and neutrino
   b. A proton becomes a neutron, creating an electron and antineutrino
   c. A neutron becomes a proton, creating an electron and neutrino
   d. A neutron becomes a proton, creating an electron and antineutrino

**Key:** D  
**Rationale:** Beta-minus or negatron decay occurs when there is an excess of neutrons in the atomic nucleus. To achieve greater stability, a neutron transforms into a proton, thereby bringing the neutron/proton ratio closer to the line of stability. To conserve charge, a negatron (electron) is created. To conserve spin/angular momentum, an antineutrino is created. The decay energy is imparted as kinetic energy split between the negatron and antineutrino.  

42. Two nuclei are isomers if they have:
   a. the same number of neutrons and protons but different energy states.
   b. a different number of neutrons but the same energy state.
   c. a different number of protons but the same number of nucleons.
   d. a different number of neutrons but the same number of protons.

**Key:** A  
**Rationale:** This is based on the definition of an isomer. When two nuclei have the same number of nucleons they are referred to as isobars. When two nuclei have the same number of protons but a different number of neutrons they are referred to as isotopes.  

43. What minimum radiation dose to the whole volume of both kidneys will likely result in nephropathy with hypertension and anemia?
   a. 20 Gy in 2 Gy/Fx
   b. 30 Gy in 2 Gy/Fx
   c. 40 Gy in 2 Gy/Fx
   d. 50 Gy in 2 Gy/Fx

**Key:** B  
**Rationale:** The kidneys are radiosensitive late responding tissues. Radiation damage develops slowly, reflective of the slow turnover of the tissue. Radiation nephropathy usually manifests as proteinuria and hypertension, with anemia. The fractionation sensitivity of the kidney is high (i.e. the $\alpha/\beta$ ratio is low). The dose tolerated by the kidney does not increase with increasing time after radiotherapy, but declines because of a continuous progression of damage, after doses well below the threshold for induction of functional deficit, which usually precludes re-irradiation. The pathogenesis of radiation nephropathy is complex. Most studies suggest glomerular endothelial injury as the start of a cascade leading to glomerular sclerosis and later tubulo-interstitial fibrosis. Several experimental studies have shown the importance of the renin–angiotensin system in the induction of glomerular sclerosis via upregulation of plasminogen activator inhibitor 1 (PAI-1) and enhanced fibrin deposition. Owing to loss of tubular epithelial cells, fibrin may then leak into the interstitium causing the onset of tubulointerstitial fibrosis. One or partial kidney irradiation can receive higher doses before damage is evident, but the whole bilateral volume is irradiated a dose of 30 Gy is sufficient to produce damage.  
44. Which factor is linked with radiation induced pneumonitis?
   a. Transforming growth factor-β1 (TGF-β1)
   b. Tumor necrosis factor-α (TNF-α)
   c. NF-kappaB (NF-kB)
   d. Interleukin-6 (IL-6)

Key: A
Rationale: Transforming growth factor beta 1 (TGF-β1) gene controls proliferation and cellular differentiation. TGF-β1 is an important modulator of the inflammatory response and in the development of tissue fibrosis in irradiated lungs. Animal and human studies have demonstrated that TGF-β1 is a major regulator of radiation-induced lung injury. Administration of anti-TGF-β1 antibodies can decrease the inflammatory response and reduce TGF-β1 activation several weeks after radiotherapy.


45. Determine the median value for the following data set: (23, 12, 77, 59, 31, 47, 48)
   a. 23
   b. 59
   c. 47
   d. 48

Key: C
Rationale: The middle value = median = 47

46. In ASCENDE-RT randomized trial comparing 3DCRT boost vs. LDR I-125 boost after 46 Gy whole pelvic EBRT, brachytherapy boost was associated with:
   a. improved biochemical PFS.
   b. worse rectal toxicity.
   c. improved urinary toxicity.
   d. no difference in biochemical PFS, rectal and urinary toxicity.

Key: A
Rationale: In ASCENDE-RT trial, brachytherapy boost was associated improved biochemical PFS but worse urinary toxicity.

47. Ovoid positioning was evaluated for the cervical cancer trials RTOG 0116 and 0128. What is the impact on LR and DFS if the ovoids are displaced away from the OS?
   a. Increase, decrease 
   b. Increase, unchanged 
   c. Decrease, increase 
   d. Unchanged, decrease 

Key: A
Rationale: Patients with displacement of ovoids in relation to the cervical os have a significantly increased risk of local recurrence with decreased DFS as evaluated in RTOG 0116 and 0128.

48. In INT-0091, what was the 5 year incidence of isolated local failure in pediatric patients with Ewing Sarcoma treated with radiation alone for local control?
   a. 2% 
   b. 9% 
   c. 16% 
   d. 23% 

Key: B
Rationale: The 5-year incidences of isolated local failure with radiation alone, surgery alone, combination surgery and radiation were 9.2%, 5.1% and 2%, respectively. However, this was not statistically significant. Moreover, the local control decision was not specified by the protocol, so there is speculation that there was an adverse selection for the patients treated with radiation alone. Further, the selection of local therapy modality does not appear to affect event free survival as even patients with localized disease are most at risk of metastatic recurrences.

49. Based on the updated results of Intergroup 0116 trial, which subset of patients with resected gastric cancer is unlikely to benefit from adjuvant chemoRT?
   a. Male 
   b. Node-positive 
   c. Intestinal histology 
   d. Diffuse histology 

Key: D
Rationale: Updated analysis of the INT 0116 trial (Smalley S, J Clin Oncol 2012) showed a benefit to adjuvant chemoradiation for most subsets, with the notable exception of patients with diffuse histology.
References: Smalley S, J Clin Oncol 2012
50. According to the International Consensus Contouring Guidelines for Adjuvant Radiation for Bladder Cancer, the superior anatomic border of the cystectomy bed CTV should extend 2 cm superior to the:
   a. initial pre-operative bladder tumor.
   b. superior aspect of the pubic symphysis.
   c. most superior placed surgical clips.
   d. inferior aspect of the sacro-iliac joint.

Key: B  
Rationale: The superior anatomic border of the contour will extend 2 cm superior to the superior aspect of the pubic symphysis.


51. Regarding the IELSG (International Extranodal Lymphoma Study Group) 10 Phase II trial for DLBCL of the testes, what was the dose to the contralateral testes DLBCL?
   a. 20 Gy
   b. 25 Gy
   c. 30 Gy
   d. 40 Gy

Key: C  
Rationale: The IELSG-10 phase II included 53 patients from age 22- with stage I or stage 2 Primary DLBCL of the testes. They were treated with 6 cycles of R-CHOP every 21 days with 4 doses of IT MTX and RT to contralateral testes (30 Gy) and to regional LNs (30-36) for stage II disease. 5 yr PFS was 74% and OS was 85%; There were no deaths as result of toxicity. Testicular RT was associated with good outcome and avoided contralateral testis relapse.

References: Vitolo U et al., JCO, 2011 July 10, 2766-72; 29(20).

52. How were the target volumes defined on the RTOG 0630 trial of pre-operative radiation and daily image guidance for extremity soft tissue sarcoma?
   a. CTV = GTV with 2 cm radial and 5 cm cranial caudal expansions
   b. CTV excluded edema seen on T2 MRI
   c. CTV expanded into bone and soft tissue
   d. GTV was defined by use of T1 weighted gadolinium enhanced MRI

Key: D  
Rationale: On RTOG 0630 trial of pre-operative radiation for soft tissue sarcoma of the extremity with daily image guidance, target volumes were defined as follows: GTV was defined by MRI T1 plus contrast images. Co-registration of pretreatment MRI and planning CT in the same position was recommended to delineate the GTV for RT planning. For intermediate to high-grade tumors >= 8 cm, CTV=GTV +3 cm margins in the longitudinal (proximal and distal) directions. The radial margin was 1.5 cm beyond the GTV. For low-grade tumors or < 8 cm, the longitudinal margin was 2 cm beyond the GTV and, the radial margin was 1 cm. The CTV was expanded to cover the suspicious edema if it extended beyond the CTV margin and was constrained by anatomic barriers, including fascia, bone, or compartment. PTV included CTV plus 5 mm for all patients.

References: Wang, D. et. al. Significant Reduction of Late Toxicities in Patients With Extremity Sarcoma Treated With Image-Guided Radiation Therapy to a Reduced Target Volume: Results of RTOG 0630 Trial. JCO 33, (2015), 231.
53. The spinal cord maximum dose constraint when planning definitive twice-daily radiotherapy for patients with limited-stage SCLC with modern radiation techniques is:
   a. 36 Gy.
   b. 41 Gy.
   c. 45 Gy.
   d. 48 Gy.

Key: B  
Rationale: Based on the CALGB 30610/RTOG 0538 protocol, the max dose constraint on the spinal cord for patients receiving definitive chemoradiation to 45 Gy in 30 fractions BID should not exceed 41 Gy.

References: CALGB/RTOG 0538 study, CALBG/RTOG protocol. NCCN 2017.

54. What percentage of oropharyngeal cancers in the United States are currently caused by HPV?
   a. <5%
   b. 5-10%
   c. 30-40%
   d. >60%

Key: D  
Rationale: Human papillomavirus (HPV) causes an epidemiologically and clinically distinct form of oropharyngeal squamous cell carcinoma (OPSCC). HPV-positive OPSCCs have risk factors related to sexual behavior whereas HPV-negative cancers are strongly associated with tobacco and alcohol use. HPV is now the major cause of oropharyngeal cancer in the United States. The incidence has increased significantly over the last 20 years.


55. Which circular electron beam field will result in the lowest relative surface dose?
   a. 6 MeV, 4 cm diameter
   b. 6 MeV, 8 cm diameter
   c. 18 MeV, 4 cm diameter
   d. 18 MeV, 8 cm diameter

Key: B  
Rationale: For electron beams, relative dose at the surface increases with beam energy. This occurs because lateral scatter reduces with increases in energy. With reduced scatter, electron fluence becomes increasingly similar between shallow regions and the depth of maximum dose (or, said differently, the relative depth-dose ratio approaches unity as incident beam energy is increased). Additionally, loss of lateral charged particle equilibrium results in increased surface dose and decreased depth of maximum dose. A rule-of-thumb for central axis equilibrium is that the field radius Req in [cm] should satisfy Req ≥ 0.88*√(E). For 6 MeV this is 2.2 cm, and for 18 MeV is 3.7 cm. Thus, option B (low energy, large field) will have the lowest relative surface dose.

56. What factor is included in the Gail model for predicting risk of developing breast cancer?
   a. Family history of ovarian cancer
   b. Number of prior breast biopsies
   c. Breast cancer in first and second degree relatives
   d. Age of onset of breast cancer

**Key:** B

**Rationale:** The Gail model was one of the initial tools that attempted to estimate a woman’s risk of developing breast cancer over the next 5 years. It considers age, race, age of first menstrual period, number of first degree relatives with a history of breast cancer, and number of prior biopsies. It is thought to underestimate the need for testing as it does not take into consideration a family history of ovarian cancer, age of onset of breast cancer, occurrence of bilateral breast cancers, history of second degree relatives with breast cancers, or the biology of the breast cancer; all important in assessing risk.


57. Which dose quantity is used to assess the radiation exposure to radiation workers?
   a. Absorbed dose
   b. Collective effective dose
   c. Dose equivalent
   d. Effective dose equivalent

**Key:** D

**Rationale:** Radiation workers are limited to an annual effective dose equivalent of 50mSv. The effective dose equivalent is used since it takes into account differences in radiation type, tissue sensitivity, and internal/external exposure.

**References:** Khan. The Physics of Radiation Therapy. Lippincott Williams and Wilkins. 2003. 3rd Ed.

58. For treatment of liver metastases with SBRT, what is the liver dose constraint for a 3-5 fraction regimen?
   a. 700 cc of liver should receive < 21 Gy
   b. 700 cc of liver should receive < 28 Gy
   c. 500 cc of liver should receive < 21 Gy
   d. 500 cc of liver should receive < 28 Gy

**Key:** A

**Rationale:** Eligible patients had one to five hepatic metastases, ability to spare a critical hepatic volume (volume receiving <21 Gy) of 700 ml, adequate baseline hepatic function, no concurrent antineoplastic therapy, and a Karnofsky performance score of ≥60. There was no grade 4 or 5 toxicity or treatment-related grade 3 toxicity.

59. What was the outcome of the POET randomized trial of preoperative chemoRT vs. preoperative chemotherapy alone for gastroesophageal junction adenocarcinoma?
   a. There was a trend towards improved survival with preoperative chemoRT
   b. There was a trend towards improved survival with preoperative chemotherapy alone
   c. There was a statistically significant survival advantage with preoperative chemoRT
   d. There was a statistically significant increase in postoperative mortality with preoperative chemoRT

Key: A
Rationale: The POET randomized trial (Stahl M et al, J Clin Oncol 2009) did not meet its target accrual. Nevertheless, there was a trend towards improved survival in the preoperative CRT group (p=0.07). There was no statistically significant different in postoperative mortality.

60. Per PORTEC-2 (Postoperative Radiation Therapy in Endometrial Carcinoma), what is the same for EBRT and vaginal brachytherapy?
   a. Long-term QoL
   b. Pelvic recurrence
   c. Vaginal cuff recurrence
   d. Acute grade 1–2 GI toxicity

Key: C
Rationale: PORTEC-2 was a randomized study that compared adjuvant external beam radiotherapy to vaginal cuff brachytherapy for patients with intermediate-risk endometrioid adenocarcinomas. While pelvic relapses were more frequent in the brachytherapy arm, vaginal recurrence rates were comparably low in both arms. The toxicity measures strongly favored brachytherapy.

61. For patients with limited stage SCLC who receive first cycle of chemotherapy prior to the start of radiation, the nodal target volume should cover:
   a. initially involved nodal region but post-induction volume.
   b. initially involved nodal region + a nodal echelon above and below.
   c. current residual nodal disease + a nodal echelon above and below.
   d. current residual nodal disease excluding nodal level with a complete response.

Key: A
Rationale: While historical nodal irradiation volumes for patients with limited stage-SCLC have extended to beyond involved nodal regions, modern series and clinical trials omit elective nodal irradiation (ENI). Further, a small randomized study reported by Hu et al., observed that irradiation of post-chemotherapy tumor extent without ENI did not have a negative impact on loco-regional control. Hence, for patients who start systemic therapy prior to the radiation therapy, the current NCCN guidelines recommend irradiation of the involved nodal region but using post-induction volume.
62. What was the conclusion from the secondary analysis of RTOG 0617 randomized clinical trial evaluating the radiation dose (60 Gy vs 74 Gy) for NSCLC?
   a. Two-year OS and PFS was superior with IMRT
   b. Lower grade ≥3 pneumonitis was seen with IMRT
   c. Lung V5 was associated with any grade ≥3 pneumonitis
   d. 3DCRT group had larger PTV: Volume of lung ratio

Key: B
Rationale: In the secondary analysis of RTOG 0617 data, the use of IMRT was associated with reduced rates of ≥ grade 3 pneumonitis (7.9% vs 3.5%, p = 0.039), reduced dose to heart without any differences in 2-year OS, PFS, local or distant failure despite having larger PTV: Volume of lung ratio. Lung V20 Gy and not V5 Gy was associated with increased ≥ grade 3 pneumonitis. Hart V40 Gy was associated with OS.

63. In the 8th edition of the AJCC Staging system, oral cavity T-category will now include which of the following?
   a. Perineural invasion
   b. Depth of invasion
   c. Lymphovascular invasion
   d. Margin status

Key: B
Rationale: The AJCC 8th edition incorporates depth of invasion (DOI) in assigning a T-category for oral cavity cancer. This recognizes the prognostic importance of a deeply invasive tumor, even if it is a small tumor. Previous staging did not include depth of invasion.

64. The tumor PD-L1 expression enrollment requirement in the KEYNOTE-010 phase 2/3 randomized study for previously treated advanced NSCLC (pembrolizumab vs docetaxel) was:
   a. No requirement.
   b. 1%.
   c. 5%.
   d. 50%.

Key: B
Rationale: To be eligible for the Keynote-010 study, patients with previously treated advanced NSCLC were required to have at least 1% tumor cells with PD-L1 expression. In the total patient population, median OS in the two pembrolizumab dose arms was significantly longer than docetaxel. In a planned subset analysis of patients with expression of PD-L1 on 50% of the tumor cells, median OS and PFS in the two pembrolizumab dose arms was significantly longer than docetaxel.
65. In patients with T1-T2 invasive breast cancer with 1 to 3 positive axillary nodes, what are the effects of postmastectomy radiation?
   a. No change in LRF, no change in breast cancer mortality
   b. No change in LRF, decreases breast cancer mortality
   c. Decreases LRF, no change in breast cancer mortality
   d. Decreases LRF, decreases breast cancer mortality

Key: D
Rationale: PMRT decreases the risk of locoregional failure, any recurrence, and also decreases breast cancer mortality. The benefit of PMRT has to be weighed against potential toxicities associated with radiation therapy.

66. In a meta-analysis of randomized trials (Auperin et al., JCO 2010), the use of concurrent chemoRT (versus sequential chemoRT) in patients with locally advanced NSCLC demonstrated:
   a. increased acute grade 3-4 esophagitis.
   b. improved LC, but not DM or OS.
   c. improved LC and DM, but not OS
   d. improved LC and OS, but not DM.

Key: D
Rationale: Concurrent chemoRT increased OS by 4.5% at 5 years (p=0.004), and decreased locoregional progression (HR 0.77 (p= 0.01). No effect (HR of 1.04) was noted on distant progression. Grade 3-4 esophagitis increased from 4% to 18% with a HR of 4.9.

67. In which part of the radiation damage response does DNA-dependent protein kinase (DNA-PKcs) primarily function?
   a. Non-homologous end joining repair
   b. Homologous recombination repair
   c. Inhibition of Rad50 activation
   d. Inhibition of p53 activation

Key: A
Rationale: There are two major types of DSB repair pathways in mammalian cells – homologous recombination repair (HRR) and non-homologous end-joining (NHEJ). A third type, single-strand annealing (SSA), shares components with both NHEJ and HRR. NHEJ uses little to no sequence homology in a process that may or may not be error-free. NHEJ requires fewer proteins than HRR. The NHEJ proteins are Ku70/80, DNA-PKcs, DNA ligase IV, and XRCC4. HRR is dependent on DNA homology and is error-free. The requirement for sequence homology is the fundamental difference between HRR and NHEJ. It is generally believed that NHEJ plays a more important role than HRR in mitotically replicating cells while HRR may play a more prominent role when sister chromatids are available during late S and G2 stages of the cell cycle. NHEJ is more important during G1 and early S phase, while HRR operates in S and G2 due to the requirement for sequence homology.
Jackson SP, Sensing and repairing DNA double strand breaks, Carcinogenesis 23, 2002; 687-696.
68. In a patient, electrons lose energy predominantly through:
   a. inelastic collisions with atomic electrons.
   b. inelastic collisions with nuclei.
   c. elastic collisions with atomic electrons.
   d. elastic collisions with nuclei.

   Key: A

   Rationale: In water or tissues, electrons lose energy predominately through inelastic collisions (ionization and excitation) with atomic electrons.


69. What were the preliminary 1 year toxicity results of RTOG 1014 trial of partial breast re-irradiation following second breast conserving surgery for recurrent breast cancer after previous breast conservation?
   a. <5% rate of grade 3 fibrosis
   b. 5% rate of grade 3 breast edema
   c. 15% rate of grade 2 chest wall pain
   d. 15% rate of grade 2 breast pain

   Key: A

   Rationale: RTOG trial 1014 evaluated partial breast re-irradiation after second lumpectomy in patients previously treated with breast conservation. A protracted hyperfractionated course of treatment was used (45 Gy in 30 fractions given bid). Treatment-related skin, fibrosis, and/or breast pain AEs were recorded as grade 1 in 64% and grade 2 in 7%, with only 1 (<2%) grade >= 3 and identified as grade 3 fibrosis of deep connective tissue.


70. Which HPV strain is MOST commonly associated with oropharyngeal cancer?
   a. HPV 8
   b. HPV 16
   c. HPV 18
   d. HPV 31

   Key: B

   Rationale: In the oropharynx, HPV 16 accounts for more than 90% of all HPV-associated cancers.


71. A recent multi-institutional analysis of brain metastases from EGFR-mutant NSCLC which examined sequencing of SRS, WBRT, and EGFR-TKI therapy, demonstrated:
   a. upfront EGFR-TKI preserves neurocognition without a detriment in OS.
   b. SRS followed by EGFR-TKI resulted in the longest OS.
   c. upfront WBRT was inferior to upfront EGFR-TKI.
   d. upfront WBRT was superior to upfront SRS.

   Key: B

   Rationale: The median OS for the SRS, WBRT, and EGFR-TKI cohorts was 46, 30, and 25 months, respectively. Upfront SRS had the best survival outcomes with improved survival in both favorable and unfavorable patient groups, when stratified by dsgP. Despite having more patients with less favorable prognosis, even on multivariate analysis upfront WBRT had improved survival over upfront EGFR-TKI (30 vs 25 months, median OS, p < 0.039). Deferring RT was associated with inferior OS.

72. During a patient-specific IMRT QA validation, a Gamma Index pass rate of 92% means:
   a. 8% of points evaluated have a gamma value of 1 or less.
   b. 92% of points evaluated have a gamma value of 0.
   c. 92% of points evaluated have a gamma value of 1 or less.
   d. 8% of points evaluated have a gamma value of 0.

   **Key:** C
   **Rationale:** When using the gamma criterion, the gamma value of each point is calculated, and the point is considered to pass the test if the gamma value is 1 or less.

73. An HDR plan was created using a source activity before a source exchange, but it will be delivered after a source exchange. What MUST be adjusted in the plan to deliver the intended dose?
   a. Increase the source dwell times
   b. Decrease the source dwell times
   c. Increase the source step size
   d. Decrease the source step size

   **Key:** B
   **Rationale:** The dose scales with the source activity and dwell times. With a higher activity source, to deliver the same total dose with the same dose distribution as the plan, but with a higher activity source, the dwell times must be reduced. If the step sizes changed, the dose distribution would change.

74. In a randomized Phase III trial (DART 01/05) using 78 Gy for prostate cancer, long-term androgen deprivation (24 months), when compared with short term androgen deprivation (4 months), was associated with a higher risk of:
   a. rectal toxicity.
   b. urinary toxicity.
   c. cardiovascular events.
   d. pulmonary toxicity.

   **Key:** C
   **Rationale:** In DART 01/05 randomized trial, LTAD did not significantly impact urinary or rectal radiation-induced toxicity but was associated with a higher risk of cardiovascular events.
   **References:** Zapatero A, Late Radiation and Cardiovascular Adverse Effects After Androgen Deprivation and High-Dose Radiation Therapy in Prostate Cancer: Results From the DART 01/05 Randomized Phase 3 Trial Int J Radiat Oncol Biol Phys, 2016;96(2): 341-348.
75. A clinical T1N0 larynx cancer does NOT require nodal treatment when it originates at which subsite?
   a. Pyriform sinus
   b. True vocal cord
   c. AE fold
   d. Laryngeal epiglottis

Key: B
Rationale: Less than 5% of patients with clinical T1 disease confined to the glottic larynx have involved lymph nodes. Therefore, the traditional small-field to treat an early-stage glottic larynx cancer does not include lymph nodes.

76. In a secondary analysis of the KEYNOTE-001 study, use of previous radiotherapy for patients with NSCLC receiving pembrolizumab:
   a. increased anemia.
   b. increased esophagitis.
   c. increased pulmonary toxicity.
   d. improved PFS and OS.

Key: D
Rationale: In patients who previously received any radiotherapy than in patients without previous radiotherapy use of pembrolizumab was associated with longer PFS (hazard ratio [HR] 0·56 [95% CI 0·34-0·91], p=0·019; median progression-free survival 4·4 months [95% CI 2·1-8·6] vs 2·1 months [1·6-2·3]) and longer OS (HR 0·58 [95% CI 0·36-0·94], p=0·026; median overall survival 10·7 months [95% CI 6·5-18·9] vs 5·3 months [2·7-7·7]). Grade ≥ 3 pulmonary toxicity with or without thoracic RT was similar (17% vs 12%). Any pulmonary toxicity was 63% vs 40% (p = 0·058). Differences in anemia or esophagitis were not reported.

77. Which chemotherapeutic agents is correctly paired with its target?
   a. Topotecan - MAPK kinase
   b. Etoposide - glutathione
   c. Bevacizumab - tyrosine kinase
   d. 5-fluorouracil - thymidylate synthase

Key: D
Rationale: 5-fluorouracil targets thymidylate synthase. Topotecan targets topoisomerase I, bevacizumab targets VEGF, and sunitib is a tyrosine kinase inhibitor which targets EFGF, VEGFR, KIT, and EGFR.
78. According to SWOG S0809, which adjuvant treatment has been established as standard-of-care for resected extrahepatic cholangiocarcinoma and gallbladder cancers?
   a. Gemcitabine+capecitabine followed by capecitabine+RT
   b. Gemcitabine followed by capecitabine+RT
   c. Cisplatin+gemcitabine+ followed by cisplatin+RT
   d. Capecitabine+oxaliplatin followed by oxaliplatin+RT

**Key:** A

**Rationale:** The trial was a phase II prospective trial of patients with resected gallbladder and extrahepatic cholangiocarcinomas (pT2-4 or N+ or positive margins, M0, performance status 0-1). Patients received gemcitabine+capecitabine followed by chemoradiation with capecitabine and RT to 54-59.4 Gy. The treatment was well-tolerated and median overall survival was 35 months, which was considered promising. This was the first multi-institutional prospective study of this disease.


79. What is the 5 year survival after laryngectomy for T4a laryngeal SCC?
   a. 5%
   b. 20%
   c. 50%
   d. 80%

**Key:** C

**Rationale:** T4a laryngeal cancer treated with laryngectomy has a 5 year survival of around 50% across multiple reports. A review of published reports showed an average survival of 46%. Laryngeal preservation in these patients has a lower overall survival and is not recommended in guidelines.


80. According to PORTEC-1, which outcome is associated with adjuvant EBRT over observation?
   a. Improved overall survival
   b. Decreased distant metastases
   c. Improved physical functioning scores
   d. Increased incontinence for urine

**Key:** D

**Rationale:** PORTEC-1 was a randomized study that compared adjuvant external beam radiotherapy to observation for select endometrioid adenocarcinomas. While local control was improved in the EBRT arm, long term follow up shows no improvement of survival by EBRT. Toxicity outcomes for EBRT are markedly worse.

**References:** Nout RA, J Clin Oncol, 2011 May 1, 29(13):1692-700.
81. According to consensus guidelines, which nodal regions should be included in the CTV for preoperative treatment of gastroesophageal junction adenocarcinoma?
   a. No elective nodal radiation is indicated
   b. Gastrohepatic nodes only
   c. Gastrohepatic and celiac nodes
   d. Gastrohepatic, celiac, and superior mesenteric nodes

**Key:** C

**Rationale:** Consensus contouring guidelines (Wu A et al., Int J Radiat Oncol Biol Phys 2015; 92:911-920) recommend routinely including the gastrohepatic nodes, which are among the most commonly involved nodes in GE junction and distal esophageal cancer. Though the rate of celiac nodes is somewhat lower, routine inclusion was recommended by the consensus panel. Superior mesenteric nodes are not considered regional nodes in esophageal cancer and are not recommended to be included routinely in the CTV.

**References:** Wu A et al., Int J Radiat Oncol Biol Phys 2015; 92:911-920.

82. With a median follow-up of 12 years, the addition of 24 months of anti-androgen therapy (peripheral androgen blockade) during and after salvage radiotherapy (RTOG 9601) significantly:
   a. A increased urinary toxicity.
   b. B improved overall survival.
   c. C increased rectal toxicity.
   d. D increased cardiovascular events.

**Key:** B

**Rationale:** With a median follow-up of 12 years, the addition of 24 months of anti-androgen therapy (peripheral androgen blockade) during and after salvage radiotherapy (RTOG 9601) significantly improved overall survival (76.3% bicalutamide group) vs 71.3% (placebo group), reduced metastatic prostate cancer, reduced death from prostate cancer, reduced local recurrence and tumor progression and no difference in toxicity.


83. Which key kinase regulator links the initial recognition of DNA double strand breaks with signaling for cell cycle arrest and break repair?
   a. ATM
   b. Cdc25A
   c. BRCT
   d. Rad51

**Key:** A

**Rationale:** The ataxia-telangiectasia-mutated (ATM) protein kinase is rapidly and specifically activated in response to DNA double-strand breaks in eukaryotic cells. MRN complex is required for ATM activation after double strand breaks (DSBs). Activated ATM then plays a role in cell cycle delay after DNA damage, especially after double-strand breaks (DSBs). ATM together with NBS1 act as primary DSB sensor proteins. These modified mediator proteins then amplify the DNA damage signal, and transduce the signals to downstream effectors such as CHK2 and p53.

84. In the COMS randomized trial of enucleation verses brachytherapy for medium choroidal melanomas, what percentage of patients developed blindness (visual acuity 20/200 or worse) in the treated eye 3 years after brachytherapy?
   a. 25%
   b. 45%
   c. 75%
   d. 95%

Key: B
Rationale: In this trial, we learned that OS was not compromised by a globe-preservation approach, with very few local failures after brachytherapy (~10%). Visual acuity diminished to 20/200 or worse in the years after brachytherapy: 17% by 1 year, 33% by 2 years, 43% by 3 years.

85. In the Phase-I RTOG 0813 study that examined SBRT for centrally located NSCLC treated in 5 fractions:
   a. the MTD was 10 Gy/ fx.
   b. the 2-year LC at the two highest dose-cohorts was 85-90%.
   c. the incidence of grade 5 toxicity at the two highest dose-cohorts was 10%.
   d. primary tumor up to 7 cm were treated.

Key: B
Rationale: Medically inoperable patients, predominantly elderly, were included in the study. The MTD in the phase I data was 12Gy/ fr x 5 fractions. The 2-year local control rates for the two highest cohorts (11.5 Gy and 12 Gy) were 89.4% (90% Cl: 81.6-97.4%) and 87.7% (90% Cl: 78.3-97%), respectively. Grade 5 toxicity attributed to SBRT was seen in 3 out of 71 patients treated at these two cohorts. T1-2 (< 5 cm) tumors were treated on this study.

86. What is included in the FLIPI Score (Follicular Lymphoma International Prognostic Index)?
   a. ESR
   b. WBC
   c. Platelets
   d. Hemoglobin

Key: D
Rationale: FLIPI is a prognostic score that was developed from large retrospective data from patients with follicular lymphoma, and includes Age > 60, Ann Arbor Stage III/IV, number of nodal sites > 4, hemoglobin, and serum LDH. Based on number of risk factors, 5 yr OS can range from 52.5% to 91% (in the pre-rituxan era); This can be used to improve treatment choices and to compare clinical trials.

87. In the CROSS trial of preoperative chemoRT vs. surgery alone for esophageal cancer, what was the approximate rate of locoregional recurrence in the chemoRT arm?
   a. 5%
   b. 15%
   c. 35%
   d. 50%

Key: B
Rationale: Analysis of patterns of recurrence in the CROSS trial (Oppedijk V et al, J Clin Oncol ’14) showed that the rate of locoregional recurrence was reduced from 34% to 14% with the use of preoperative chemoradiation. (p<0.001).
88. What is the shape of the excess relative risk dose response for solid tumors in females from the Life Span study of atomic bomb survivors?
   a. Linear-quadratic with no threshold
   b. Linear-quadratic with a threshold
   c. Linear with no threshold
   d. Linear with a threshold

Key: C
Rationale: The most recent results from the Life Span study of atomic bomb survivors (1958-2009) indicates a linear dose response for excess relative risk of solid tumor formation in females. This response has no threshold. Contrary to previous results, the male data was best fit by a linear-quadratic model also with no threshold. The Radiation Effects Research Foundation (RERF) is being cautious about inferring what this result means and has adapted a conservative approach with regard to setting radiation safety limits. They believe that further study is necessary before making any changes to currently accepted standards.


89. Which sequence BEST describes the DECREASING radiosensitivity of late-responding normal tissues to TBI?
   a. Lung, Liver, Kidney
   b. Lung, Kidney, Liver
   c. Liver, Kidney, Lung
   d. Liver, Lung, Kidney

Key: B
Rationale: The lung is amongst the most radiosensitive of the late-responding normal tissues. Two waves of damage are evident: acute pneumonitis at 2 to 6 months post treatment and later fibrosis from months to years post irradiation. The functional subunit in the lung is the pulmonary lobule, and these are arranged in parallel and therefore volume irradiated and dose are important in radiation response of the lung. The kidney is also a sensitive late responding tissue with FSUs arranged in parallel and damage develop slowly and is irreversible. The liver is not as radiosensitive as the kidneys or lungs, it FSUs are also arranged in parallel and therefore larger doses can be tolerated if the irradiated volume is small Liver tolerance is only dose limiting if the whole organ is irradiated.


90. How does the sensitivity of proton beams to tissue heterogeneities compare to that of photon beams?
   a. Less sensitive
   b. More sensitive
   c. No difference
   d. Depends on beam energy

Key: B
Rationale: Proton beams are more sensitive to tissue heterogeneities because small changes to density will have a large impact on the dose due to the final location of the Bragg Peak.

91. Higher prevalence of basal-like breast cancer is associated with which risk factors or patient subgroups?
   a. Breast feeding
   b. Low BMI
   c. Premenopausal African American women
   d. Postmenopausal Caucasian women

**Key:** C

**Rationale:** Basal-like breast tumors occurred at a higher prevalence among premenopausal African American patients compared with postmenopausal African American and non-African American patients in this population-based study. Breast feeding was associated with reduced risk of basal like breast cancer. Obesity with associated with increased risk of basal-like breast cancer in pre- and postmenopausal women. **References:** Carey, LA et. al., JAMA. 2006; 295(21): 2492. Millikan, RC et. al., Breast Cancer Research and Treatment. 2008; 109(1): 123

92. For treatment of primary CNS lymphoma, what is the minimum dose of methotrexate needed to cross the blood-brain barrier?
   a. 0.5 g/m2
   b. 1.0 g/m2
   c. 3.0 g/m2
   d. 8.0 g/m2

**Key:** C

**Rationale:** Doses above 3.0 to 3.5 g/m2 are enough to cross the blood brain barrier. **References:** Hoang-Xuan, Lancet Oncol, 2015 Jul, 16(7):e322-32.

93. Based on NCRP, what is the total dose limit for the fetus of a pregnant radiation worker?
   a. 0.05 mSv
   b. 0.5 mSv
   c. 5 mSv
   d. 50 mSv

**Key:** C

**Rationale:** According to the guidelines of the NCRP Report No.91, the fetus can receive a maximum of 5 mSv over the whole course of pregnancy. **References:** Report 91 of the NCRP. NCRP. 1987.

94. Which change has been incorporated into the AJCC Staging 8th edition for breast cancer?
   a. Tumor marker levels
   b. Multigene recurrence score
   c. Lobular carcinoma in situ
   d. Phyllodes tumor

**Key:** B

**Rationale:** There are many changes to breast cancer staging in the AJCC 8th edition including anatomic stage group and prognostic stage group, incorporation of biomarkers such as ER/PR/Her2 status, grade, and recurrence scores. Lobular carcinoma in situ (LCIS) has been removed from AJCC breast staging and is no longer Tis as it is treated as a benign entity. Breast sarcomas, phyllodes tumors, and breast lymphomas are not included in the breast cancer staging system. Tumor markers are not included in the staging system. **References:** AJCC 8th edition MB Amin editor in chief 2016, Springer International Publishing.
95. Which en-face electron beam energy is preferable to spare an organ at risk (OAR) at a depth of 5 cm?
   a. 9 MeV
   b. 12 MeV
   c. 16 MeV
   d. 20 MeV

Key: A
Rationale: The range of an electron beam is given by E/2. To spare something at a depth of 5 cm, only the 9 MeV beam works (range of 4.5 cm)

96. What does the term “uterine junctional zone” refer to in MRI imaging?
   a. Contrast enhancement of the serosal lining
   b. High T2 signal corresponding to the endometrium
   c. Intermediate T2 signal of the outer myometrium
   d. Low T2 signal of the innermost myometrium

Key: D
Rationale: Junctional zone is a distinct area of low (bright) T2 signal in the uterus on pelvic MRI. It has been histologically correlated to the inner myometrium (i.e. situated just deep to the endometrium). Careful examination of the junctional zone appearance is helpful in the evaluation of the inoperable endometrial cancer. Breach or interruption of the junctional zone differentiates between tumors confined to the endometrium and those invading the myometrium.

97. What is the MOST appropriate timing, dose and means of radiotherapy for a 4 mm unilateral retinoblastoma without extra-ocular extension?
   a. Up front EBRT to 45 Gy in 25 fractions
   b. Consolidative plaque brachytherapy prescribed to 5mm to 36 Gy after systemic chemotherapy +/- other focal therapies
   c. Consolidative EBRT to 36 Gy in 20 fractions after systemic chemotherapy +/- other focal therapies
   d. Up front plaque brachytherapy prescribed to 5mm to a dose of 50 Gy

Key: B
Rationale: Episcleral plaque brachytherapy is preferred for localized tumors without extraocular extension or vitreous seeding when other focal therapies (diode, laser, cryo) and chemotherapy have failed to cause complete regression of the primary mass.
98. In which phase of the cell cycle are cells most sensitive to hyperthermia-induced cell killing mechanisms?
   a. G1
   b. S
   c. G2
   d. M

Key: B
Rationale: Hyperthermia is most effective at killing S phase cells, while S phase cells are most resistant to radiation-induced cell killing. Hyperthermia is most effective radiosensitizer if given at the time of radiation. However, the best therapeutic effective is achieved using sequential heat treatment rather than simultaneous treatment. Sequential treatment spares normal tissue injury because of differences in blood flow between tumor and normal tissues.

99. For a parallel-opposed, open field tangential breast plan, the lateral jaw is increased by 5cm to enhance the beam flash. What is the expected effect on the beam MUs?
   a. Increase by ~10%
   b. Increase by ~3%
   c. Decrease by ~3%
   d. Decrease by ~10%

Key: C
Rationale: As the field size is increased, the total scatter factor increases and the MUs will decrease for a fixed dose at depth. The change in total scatter factor from a 10x10 to a 30x30 field is less than 8% so a decrease of 10% is not likely.

100. Which side effect is associated with improved OS in patients receiving RT and cetuximab for head and neck cancer?
   a. Desquamation
   b. Pruritus
   c. Erythema
   d. Acneiform rash

Key: D
Rationale: In a landmark phase III trial, patients with head and neck cancer undergoing definitive treatment with concurrent radiation therapy and cetuximab, patients who developed a grade 2 or greater acneiform rash had an improved overall survival when compared to patients with either no rash or a grade 1 rash.
101. A patient presents with a 4 cm right neck mass, progressive left maxillary formication sensation, and left retro-orbital pain. Right neck FNA demonstrates nasopharyngeal carcinoma. PET-CT shows uptake in the right neck mass and nasopharynx, with no evidence of distant metastases. How is this patient staged? (The staging is the same per 7th and 8th editions)
   a. T4aN1M0
   b. T4aN2aM0
   c. T4N1M0
   d. T4bN2aM0

Key: C
Rationale: T4 designation, based here on cranial nerve involvement, is not subdivided for NPC. The upper bound for N1 disease is 6 cm.

102. Which photon interaction is most probable in the patient when performing a MV portal image for pre-treatment patient alignment?
   a. Photoelectric
   b. Compton scattering
   c. Pair production
   d. Rayleigh scattering

Key: B
Rationale: For a megavoltage beam produced by a linear accelerator for portal imaging (e.g. 6 MV), Compton scattering is the most probable interaction. This beam energy is well above the atomic electron binding energies that are responsible for the photoelectric effect, and below that required to produce substantial pair production. Rayleigh or coherent scattering is a small component of all photon interactions in radiotherapy and becomes appreciable only for very low energy photons in high atomic number materials.
103. Which oncovirus is associated with the development of Kaposi’s Sarcoma?
   a. Epstein-Barr virus
   b. Human papillomavirus
   c. Human herpesvirus 8
   d. Human lymphotrophic virus

Key: C


Rationale: The presence of human herpesvirus 8 or Kaposi’s sarcoma-associated herpesvirus (KSHV) is a primary and necessary factor in development of Kaposi’s sarcoma. KSHV is also associated with primary effusion lymphoma and multicentric Castleman’s disease. Epstein-Barr virus (EBV) or human herpesvirus 4 is associated with Burkitt’s lymphoma and nasopharyngeal carcinoma. Human T-lymphotropic virus is associated with adult T-cell leukemia.

104. A slowly proliferating tumor has an α/β ratio of 1.5 Gy. Dose-limiting normal tissue has an α/β ratio of 5 Gy. Which fractionation schedule would likely result in the highest therapeutic ratio?
   a. Standard fractionation
   b. Accelerated treatment
   c. Split-course treatment
   d. Hypofractionation

Key: D

Rationale: A hypofractionated treatment regimen who result in the highest therapeutic ratio since the tumor (α/β ratio=1.5 Gy) would be spared at a greater rate than the dose-limited normal tissue (α/β ratio = 5 Gy). A split-course treatment would not be beneficial since the α/β ratio indicates there would be greater recovery in the tumor as compared to the normal tissue, and accelerated treatment would not be indicated since the tumor is relatively slow-growing (Tpot= 35 days).


105. A grade III glioma is histologically consistent with an astrocytoma and has 1p19q co-deletion and IDH mutation. How should this tumor be classified according to the 2016 WHO classification?
   a. Anaplastic astrocytoma
   b. Anaplastic oligodendroglioma
   c. Anaplastic ependymoma
   d. Glioblastoma

Key: B

Rationale: In the 2016 WHO Classification of Brain Tumors, at times molecular type determines the diagnosis rather than classic histology on H&E. A histologic astrocytoma, but a molecular oligodendroglioma (with IDH mutation and 1p19q co-deletions), is an oligodendroglioma. Similarly, a histologic oligodendroglioma but without 1p19q co-deletion is not an oligodendroglioma, assuming the molecular testing is accurate. A glioblastoma (GBM) is not a grade III tumor.

106. What is the typical consolidation radiation dose for DLBCL after complete response to chemotherapy?
   a. 20 Gy
   b. 30 Gy
   c. 40 Gy
   d. 50 Gy

   **Key:** B
   **Rationale:** The recommended dose after consolidation for CR for DLBCL after chemotherapy is 30-36 Gy; For PR, it is 40-50 Gy; For primary treatment for refractory or non-candidates for chemotherapy, it is 40-55 Gy;

107. What is the goal of neoadjuvant chemotherapy for patients with bilateral Wilms tumor?
   a. Reduced risk of local, regional and distant recurrence
   b. Permit omission of whole lung irradiation
   c. Permit partial nephrectomy
   d. Reduce flank irradiation field size

   **Key:** C
   **Rationale:** Neoadjuvant chemotherapy is primarily utilized to permit a nephron sparing approach given that end stage renal failure may occur in as much as 12 % of cases and is thus a major source of morbidity in this population. Response based omission of whole lung irradiation is not a goal of AREN 0534. Flank radiation fields remain the same size regardless of response to neoadjuvant chemotherapy. Neoadjuvant chemotherapy has not been shown to more effectively reduce the risk of local, regional or distant recurrence relative to adjuvant chemotherapy.

108. What is the contralateral lung dose constraint when using IMRT after extrapleural pneumonectomy?
   a. V20 <35%
   b. V20 <20 %
   c. Mean lung dose <15 Gy
   d. Mean lung dose <8.5 Gy

   **Key:** D
   **Rationale:** In the early MDACC IMRT experience, fatal pulmonary death was seen in ~10% of patients. Risk of pulmonary related death with a V20 of >7% was 42-fold higher and mean lung dose (MLD) of >8.5 Gy was 8.6-fold. The authors concluded to keep V20 < 7% and MLD < 8.5 Gy.

109. On the COG protocol D9803 for patients with intermediate risk rhabdomyosarcoma, what factor was associated with an increased risk of local failure?
   a. Size > 5 cm
   b. Positive lymph nodes
   c. Parameningeal site
   d. Alveolar histology

   **Key:** A
   **Rationale:** Only size was associated with an increased risk of local failure. 5y local failure for tumors >= 5cm was 25% vs. 10% for tumors < 5 cm (p = 0.0004) Histology, nodal status, and site were not associated with an increased risk of local failure.
110. What is the appropriate adjuvant radiation after resection of a 4 cm favorable histology Wilms tumor that did not extend beyond the kidney, with tumor spill throughout the abdomen?
   a. Flank radiation to 10.8 Gy
   b. Flank radiation to 19.8 Gy
   c. Whole abdomen radiation to 10.5 Gy
   d. Whole abdomen radiation to 19.5 Gy

**Key:** C  
**Rationale:** Patients with diffuse spill (or pre-operative rupture) have Stage III disease and require whole abdomen radiation therapy. The dose for whole abdomen radiation in patients with favorable histology is 10.5 Gy in 7 fractions. Patients with favorable histology Wilms tumor and Stage I or II disease do not require adjuvant radiation therapy. There are a number of scenarios in which flank radiation is indicated, such as Stage I Wilms with unfavorable histology. Whole abdomen to 19.5 Gy can be used in cases of diffuse peritoneal implants.


111. Immunotherapy has been shown to be potentially effective in:
   a. microsatellite stable colon cancer.
   b. microsatellite unstable colon cancer.
   c. pancreatic cancer.
   d. gallbladder cancer.

**Key:** B  
**Rationale:** A phase II study of pembrolizumab 10 mg/m2 every 14 days for microsatellite stable and unstable colon cancer demonstrated an objective response rate of 0% vs. 40%, respectively. To date, there has been little reported response to immunotherapy drugs among pancreatic and gallbladder cancer, although trials are underway.


112. How many mitotic figures per 10 HPF (high power field) define grade III meningiomas?
   a. ≤4
   b. 5-9
   c. 10-19
   d. ≥20

**Key:** D

**Rationale:** Meningiomas are graded by mitotic activity, among other features. Grade III meningiomas have 20 or more mitotic figures per 10 HPF.


113. A two-armed clinical trial randomized 40 subjects into group A or group B, and the outcome of interest is the change in serum cholesterol. The observed mean difference of the changes between two groups is 2.5mg/dl. What additional information is needed to determine the difference between the two arms?
   a. Median
   b. Standard Deviation
   c. Range
   d. Variance

**Key:** B

**Rationale:** In order to answer this question, we need to know the standard deviation of the difference of change in serum cholesterol between two groups. If the standard deviation is given, we can derive 95% confidence interval of the difference between two treatments. If the 95% confidence interval does not contain 0, then we reject the null hypothesis and make the conclusion—there is statistical difference between the treatments.

**References:** https://onlinecourses.science.psu.edu/stat509/node/27.
114. What is a consequence of contouring the target volume on a misregistered MRI (incorrectly aligned to simulation CT) during treatment planning?
   a. Different dose resolution within the target
   b. Incorrect set up margin expansion
   c. Hot spots within the target volume
   d. Geographic miss of the target

Key: D
Rationale: If a target volume is inaccurately contoured on the CT (not MR), it could result in a geographic miss.

115. Regarding the NSABP analysis of 21-Gene Recurrence Score Assay, what is the relationship between the recurrence score and locoregional recurrence at 10 years?
   a. Age was not a significant risk factor for LRR on multivariate analysis.
   b. For patients with low recurrence scores (<18) who did not receive any systemic therapy, the LRR was 5-10%.
   c. The supraclavicular fossa was the most common site of regional failure.
   d. For patients treated with chemotherapy and tamoxifen, the LRR was < 10% regardless of score.

Key: D
Rationale: Age < 50 was a significant risk factor for locoregional recurrence with a p-value of 0.0002 and HR of 0.4. Placebo treated patients with low Oncotype scores had a LRR risk of 10.8%. The axilla was the most common site of regional failure. LRR risk ranged from 1.6 – 7.8% between the low and high-risk groups.

116. What type of clinical trial evaluates the efficacy and toxicity of a drug after post-market approval?
   a. Phase I
   b. Phase II
   c. Phase III
   d. Phase IV

Key: D
Rationale: A Phase IV clinical trial is a post-marketing surveillance study to evaluate the real-world effectiveness of a drug in an observational, non-interventional setting complementing the efficacy determined by pre-marketing randomized trial.

117. For a TG-51 calibration of a 6 MeV electron beam using a parallel-plate chamber, where is the effective point of measurement located?
   a. Top surface of the collection volume
   b. Between the top surface and center of the collection volume
   c. Center of the collection volume
   d. Bottom surface of the collection volume

Key: A
Rationale: The effective point of measurement for a parallel-plate chamber is at the top surface of the collection volume.
118. After a radical inguinal orchiectomy for a stage I seminoma, pathology demonstrates a 3.4 cm tumor with rete testis involvement, no LVSI and a negative spermatic cord margin. What is the risk of relapse with surveillance?
   a. 5%
   b. 12%
   c. 16%
   d. 30%

**Key:** C  
**Rationale:** After radical surgery, multiple prognostic factors have been identified that are associated with risk of relapse if no further adjuvant therapy is given. These include size > 4cm, LVSI, and rete testis involvement. Relapse risk is as follows: No risk factors: 12%; 1 risk factor: 16%; 2 risk factors: 30%.


119. Which mechanism is involved with silencing oncogene expression?
   a. Gene amplification  
   b. Point mutation  
   c. DNA methylation  
   d. Chromosomal translocation

**Key:** C  
**Rationale:** DNA methylation is associated with the silencing of gene expression and is typically associated with tumor suppressor gene silencing. Gene amplification, point mutations and chromosomal translocations are all associated with excess normal protein expression or abnormal (hyperactive) protein expression which are key features on oncogenes.


120. From Japanese bomb survivors' data, what radiation effect was seen for embryos irradiated beyond 20 weeks gestation, compared with 7 week gestation?
   a. Increased risk of malignancy  
   b. Smaller stature  
   c. Pronounced microcephaly  
   d. Lower risk of retardation

**Key:** D  
**Rationale:** The effects of radiation to the embryo and fetus depend upon the stage of gestation, the dose, and the dose rate. Congenital malformations are seen with radiation in the early (2-6 weeks) phases of development. Severe mental retardation is nearly 4 times more common if the radiation is received between 8 and 15 weeks than if it is received later. Children exposed in utero are shorter, lighter, and have a smaller head diameter than those not exposed to radiation.

121. In patients treated with prior mastectomy and axillary nodal staging and no post mastectomy radiation, where is the most common site of locoregional recurrence?
   a. Chest wall
   b. Axillary lymph nodes
   c. Internal mammary nodes
   d. Supraclavicular nodes

Key: A

Rationale: The most frequent site of locoregional recurrence after mastectomy without post mastectomy radiation is the chest wall, followed by the axillary and supraclavicular nodal regions. Following LRR, rates of subsequent metastases are high, indicating many women with LRR with die of breast cancer. On multivariate analysis nodal failures (as compared to chest wall recurrences) and disease-free interval less than 2 years were unfavorable. Those women treated with both surgery and RT had improved loco-regional control from women treated with a single modality.


122. Which clinical or pathologic feature would meet eligibility criteria for the RTOG 9804 trial of radiation versus observation for good-risk DCIS?
   a. Small palpable breast mass
   b. Multicentric calcifications
   c. 2 cm intermediate grade
   d. 2 mm margins

Key: C

Rationale: Eligibility for RTOG 9804 included: women with DCIS detected by mammogram or incidentally found in tissue of an otherwise benign biopsy; unicentric, low or intermediate nuclear grade DCIS less than 2.5 cm; with minimal margin width of 3 mm. All patients had a negative post-excision mammogram. Patients were randomized to breast RT versus no RT. With a median follow up of 7 years, 7-year risk of in-breast recurrence was 6.7% with no RT and 0.9% with RT.


123. Which laboratory assay measures in vivo local control of a cancer by radiation (or chemoRT)?
   a. Tail vein injection assay
   b. TCD50 assay
   c. Wound healing assay
   d. Spheroid growth assay

Key: B

Rationale: Tail vein injection assays are designed to assess the ability of a cell to extravasate from the bloodstream and develop metastatic deposits. Wound healing assays are in vitro assays that investigate the ability of a cell to migrate across a “wound.” Spheroid growth assays assess the growth of tumor cell in three-dimensional in vitro culture. TCD50 assays are used to determine the dose of radiation required to achieve local control in 50% of tumors.

124. What was the peak latent period for leukemia induction seen in the Japanese bomb survivors?
   a. 1-3 years
   b. 5-8 years
   c. 10-13 years
   d. 15-18 years

Key: B
Rationale: The latent period is the time between radiation exposure and the appearance of the malignancy. For the Japanese atomic bomb survivors the incidence of leukemia reached a peak in 5 to 7 years with most cases reported before 15 years since the attack.

125. When using brachytherapy as a boost treatment for vaginal cancer, what is the maximum tumor thickness for which an intracavitary cylinder implant can be used?
   a. 5 mm
   b. 10 mm
   c. 15 mm
   d. 20 mm

Key: A
Rationale: Residual vaginal tumors less than 5 mm thickness can be treated with intracavitary vaginal brachytherapy. Thicker tumors should be considered for interstitial if using brachytherapy as a boost.

126. A patient had a partial glossectomy and neck dissection for T2N1 squamous cell carcinoma of the oral tongue with extranodal extension. Which is the most appropriate adjuvant treatment?
   a. Radiation therapy
   b. Radiation therapy and concurrent chemotherapy
   c. Chemotherapy
   d. Radiation therapy followed by sequential chemotherapy

Key: B
Rationale: The RTOG 9501 and EORTC 22931 trials compared adjuvant radiation therapy versus adjuvant radiation therapy and concurrent bolus cisplatin in resected head and neck squamous cell carcinoma. The combined analysis showed an overall survival benefit for patients with positive margins and extranodal extension.

127. What is the approximate 5-year local regional failure rate of T4, node positive anal cancer after definitive chemoRT?
   a. 20%
   b. 40%
   c. 60%
   d. 80%

Key: C
Rationale: According to the secondary analysis of RTOG 98-11 stratified by TN staging, for patients with T4, N1-3 cancer, the rate of 5 year LRF was 60%.
128. What is the front line therapy for stage IE or IIE, H. pylori positive, t(11:18) positive, gastric MALT?
   a. Induction chemo-immunotherapy
   b. IFRT
   c. Antibiotics
   d. Resection

   **Key:** C
   **Rationale:** Antibiotics (C) are still given up front, to see if there is resolution, even if there is t(11:18) translocation, which predicts for poor response to antibiotics. ISRT (not IFRT) is considered for persistent disease after antibiotics. Rituxan is only considered, if ISRT is contraindicated. Gastrectomy/Resection was replaced by radiotherapy and would be too morbid.

129. What is the approximate rate of pathologic complete response in gastric patients undergoing preoperative chemoRT with 45Gy and concurrent 5 FU and cisplatin therapy?
   a. 2%
   b. 10%
   c. 25%
   d. 50%

   **Key:** C
   **Rationale:** The RTOG 9904 trial was a phase II trial of preoperative chemoRT, for which the primary endpoint was pathologic complete response rate. A pCR rate of 26% was observed
   **References:** RTOG 9904.

130. Compared with definitive penectomy, organ preservation with brachytherapy for penile cancer results in:
   a. comparable local control and OS.
   b. decreased local control but comparable OS.
   c. comparable local control and DFS.
   d. decreased local control but comparable DFS.

   **Key:** B
   **Rationale:** Based on a 2015 meta-analysis, both penectomy and brachytherapy result in good and comparable overall survival, though penectomy did have a statistically significant advantage in disease free survival and local control at 5 years. The organ preservation rate for brachytherapy was 74%.

131. A lung lesion with a PTV of 35 cm³ is treated with a SBRT technique. For a high-quality plan, the ratio of the 50% prescription isodose volume to the PTV (R50%) is expected to be closest to:
   a. 2.
   b. 4.
   c. 8.
   d. 10.

   **Key:** B
   **Rationale:** Based on most SBRT lesions, the R50% ranges from 5 to 3 for volumes 7cc to 126cc, respectively.
   **References:** Videtic, GM. RTOG 0915. NRG Oncology.
132. What is an appropriate RAI dose for metastatic papillary thyroid cancer after thyroidectomy?
   a. 25 mCi
   b. 60 mCi
   c. 150 mCi
   d. 300 mCi

**Key:** C

**Rationale:** For patients with confirmed radioiodine-avid metastatic disease, doses between 100 and 200 mCi are recommended.

**References:** NCCN Guidelines Thyroid Carcinoma, 2016. PAP-7, NCCN, 1.2016.
Cooper et al., Revised American Thyroid Association management guidelines for patient with thyroid nodules and differentiated thyroid cancer, Thyroid, 19(11), PMID: 198605772009. 1167-214.

133. Per the KEYNOTE-012 study, which agent was approved for treatment of recurrent or metastatic, PD-L1 positive, head and neck SCC?
   a. Brentuximab
   b. Ipilimumab
   c. Cetuximab
   d. Pembrolizumab

**Key:** D

**Rationale:** The KEYNOTE-012 study was an open-label, multicenter, phase 1b trial of patients with recurrent or metastatic squamous cell carcinoma of the head and neck. Pembrolizumab is an anti PD-1 antibody, and the study was limited to patients with cancers that expressed PD-L1. The proportion of patients with an overall response was 18%. In response to these results, the Food and Drug Administration (FDA) approved pembrolizumab on August 5 for the treatment of these select patients with advanced head and neck cancer.


134. What was the 5 year failure-free survival for patients with low risk Group III orbital embryonal rhabdomyosarcoma with less than complete response to induction chemotherapy treated with 45 Gy on ARST0331?
   a. 76%
   b. 84%
   c. 92%
   d. 100%

**Key:** B

**Rationale:** Patients with CR to induction chemotherapy had 100% FFS at 5 years compared to 84% for patients with less than a CR (p=0.11). Although these rates were not significantly different, these results suggest that 45 Gy may not be sufficient for patients with less than a CR after treatment with the modest doses of cyclophosphamide used on the low-risk study.

**References:** Ermoian, et al., Pediatric Blood and Cancer 45 Gy is not sufficient radiotherapy dose for Group III orbital embryonal rhabdomyosarcoma after less than complete response to 12 weeks of ARST0331 chemotherapy: A report from the Soft Tissue Sarcoma Committee of the Childrens Oncology Group, (2017)
135. What is assessed to determine the extent of radiobiological damage in the jejunum?
   a. The number of regenerating crypts
   b. The number of shortened villi
   c. The density of cells in the surface membrane
   d. The density of cells in the inner membrane

Key: A
Rationale: In the small intestine one of the first effects within the epithelium after irradiation is that of stem cell apoptosis, evident within a few hours of even low-dose irradiation. Stem cell death will not produce GI acute radiation syndrome unless the dose is sufficiently large to eliminate all the stem cells, such that there is no regeneration of the tissue and therefore tissue function is lost. For GI syndrome, this requires death of the extended clonogenic cell populations. A hierarchical response to radiation has been proposed within the clonogenic cell population, with increasing doses of radiation targeting successive tiers of clonogens within each intestinal crypt. The score of radiation damage is therefore determined by assessing the number of regenerating crypts per circumference of the sectioned jejunum. The number of crypts is plotted against as a function of dose to determine clonogenic survival.


136. What margin dose is appropriate for SRS of a non-functioning pituitary adenoma?
   a. 8 Gy
   b. 14 Gy
   c. 24 Gy
   d. 36 Gy

Key: B
Rationale: The stereotactic radiosurgery dose or Gamma Knife dose for non-functioning pituitary adenomas is approximately 14-18 Gy.


137. What is the expected biochemical RFS rate with salvage brachytherapy in the setting of biochemical failure after high-dose EBRT for prostate cancer?
   a. 30%
   b. 50%
   c. 70%
   d. 90%

Key: C
Rationale: Phase II data has demonstrated that salvage brachytherapy after external beam radiation to a median of 81 Gy is effective and safe, and results in a 5 year biochemical relapse-free survival of 68.5%.

**138.** What is a major advantage of ultrasound based IGRT?
   a. Uses no ionizing radiation  
   b. Can be used for any treatment site  
   c. Does not require any special training for use  
   d. Ultrasound systems require minimal QA

*Key: A*


*Rationale:* Since ultrasound does not require ionizing radiation, it can be used for large amounts of time. However, it does require training and on-going QA and does not work where there is bone or air in the path of the beam.

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**139.** Which organ is LEAST likely to tolerate 70 Gy in 35 Fx delivered to 5% of its volume?
   a. Heart  
   b. Spinal Cord  
   c. Lung  
   d. Liver

*Key: B*

*Rationale:* The Functional subunits in the spinal cord are arranged in serial pattern, therefore irradiation of a small volume of the spinal cord to 70 Gy can cause myelopathy. For organs with FSU arranged in parallel inactivation of a single FSU can compromise the function of the entire organ. In comparison, FSUs in the lung, liver and heart are arranged in parallel, meaning that these organs have a large functional reserve and therefore can tolerate high doses provided the irradiated volume is small.


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**140.** What is the approximate minimum energy to produce an ionizing event?
   a. 4.9 eV  
   b. 25 eV  
   c. 10 keV  
   d. 100 keV

*Key: B*

*Rationale:* Since different molecules and atoms ionize at different energies, the boundary of ionization is between 10 eV and 33 eV. 4.9 eV is the energy required to break a C=C bond, 100 keV is the energy required for Compton scattering and 10 keV is associated with photoelectric absorption.


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**141.** After receiving 50 Gy to the pelvis for prostate cancer using EBRT, what is the appropriate brachytherapy boost dose using Iodine-125?
   a. 90 Gy  
   b. 110 Gy  
   c. 125 Gy  
   d. 145 Gy

*Key: B*

*Rationale:* Brachytherapy doses using Iodine-125 are as follows – 145 Gy as monotherapy, 110 Gy as a boost dose following external beam radiation. Brachytherapy doses using Palladium-103 are as follows – 125 Gy as monotherapy and 90-100 Gy as a boost dose following external beam radiation.

*References:* NCCN Guidelines v.2.2017 – Prostate Cancer.
142. The first echelon draining lymphatic region for cancers of the bulbous urethra is:
   a. external iliac.
   b. internal iliac.
   c. presacral.
   d. inguinal.

Key: D
Rationale: Cancers of the Bulbous Urethra are the most common and are considered to originate in the anterior urethra, which along with the penile urethra and the distal widening, known as the Fossa Navicularis, drain into the superficial and deep inguinal lymph nodes. Cancers of the posterior urethra, including those of the Membranous and Prostatic Urethra drain into the external and internal iliac nodes as well as the presacral lymph nodes.

143. What is the MOST common childhood malignancy?
   a. Glioma
   b. Sarcoma
   c. Leukemia
   d. Neuroblastoma

Key: C
Rationale: Of children ages 0 – 19 years, leukemia is the most common childhood malignancy. Neuroblastoma is the most common malignancy of infants.

144. In ACOSOG Z011, a randomized trial of sentinel lymph node biopsy alone vs. completion axillary lymph node dissection (ALND) in cT1-2N0 breast cancer:
   a. there was a statistically significant decrease in nodal recurrences for patients undergoing ALND.
   b. axillary ultrasound was required prior to surgery.
   c. patients with 3 or more positive LNs were deemed ineligible and underwent ALND.
   d. extended nodal irradiation was allowed for patients with more than two positive LNs.

Key: C
Rationale: A is false, p-value was 0.28.
B is false, axillary ultrasound was not a required part of the work-up.
D No extended field radiation was permitted although there were protocol deviations.
145. Cells irradiated in the G1 phase of the cell cycle are primarily influenced by the action of p53 and which other cell cycle regulatory protein?
   a. A Cyclin A
   b. B p21
   c. C Cdc25c
   d. D Chk1/2

Key: B
Rationale: DNA damage response involves activation of cell cycle checkpoints that causes a delay in the movement of cells through the phases of the cell cycle. The G1 arrest triggered by the ionizing radiation occurs largely through the transactivation of p21Waf1 by p53, which inhibits G1 cyclin-dependent kinases, maintains the Rb-E2F complex, and consequently prevents S phase entry, thus halting the damaged cells from undergoing DNA replication.

p21Waf1 was identified as the means by which p53 induces G1 arrest, because it contains p53-binding elements in its promoter.

Fei P and El-Deiry WS., P53 and radiation responses, Oncogene. 2003 Sep 1;22(37):5774-5783.

146. For a population of data, which statistical measure decreases as the number of samples increases?
   a. Mean
   b. Standard error of the mean
   c. Standard deviation
   d. Variance

Key: B
Rationale: The standard error of the mean is the standard deviation of the distribution divided by the square root of the sample size. The greater the dispersion around the mean (standard deviation), the less certain the population mean and the greater the standard error of the mean. The larger the sample size the more confidence of the mean, the smaller the standard error of the mean.


147. On the NSABP pooled analysis of breast cancer patients treated with neoadjuvant chemotherapy and lumpectomy, which factors were associated with locoregional recurrence (LRR) risk?
   a. Age, cN status, pN status
   b. Age, cT status, pN status
   c. cT status, pT status, pN status
   d. cT status, cN status, pN status

Key: A
Rationale: A combined analysis of results from the NSABP B-18 and B-27 trials was used to evaluate predictors of locoregional recurrence after neoadjuvant chemotherapy. For patients treated with lumpectomy: age, clinical nodal status, and pathologic nodal status/breast response were predictors of LRR. For patients treated with mastectomy: clinical tumor size, clinical nodal status, and pathologic nodal status/breast tumor response were predictors of LRR.

148. Three randomized trials (CHHiP, PROFIT and RTOG 0415) comparing conventional fractionation vs. hypofractionation regimens for prostate cancer have shown that hypofractionation regimen is _____ to conventional fractionation in 5 year DFS.
   a. Superior
   b. Inferior
   c. Non Inferior
   d. Non Superior

Key: C
Rationale: All three trials have non-inferiority design showing hypofractionation regimen is non-inferior to standard fractionation regimen.

149. The frequencies of which chromosome biomarker are expected to be stable and can be used in retrospective dosimetry?
   a. Dicentric
   b. Ring
   c. Translocation
   d. Acentric fragment

Key: C
Rationale: While biological dosimetry based on the frequencies of dicentrics is useful immediately after accident, for retrospective estimation after several months the frequencies of dicentric is not used because they are unstable and lead to cell death. Unlike unstable dicentrics, chromosome translocations are expected to be stable and their frequencies can be used in retrospective dosimetry. Radiation-induced rings are also unstable and therefore not unsuitable for retrospective dosimetry. Acentric fragments can be stable or lost from the cell during cell division and are therefore not unsuitable for retrospective dosimetry.

150. What is the MOST common site of MALT?
   a. Orbit
   b. Stomach
   c. Parotid Gland
   d. Small Bowel

Key: B
Rationale: The most common site for MALT is the stomach. Stomach does not normally contain lymphoid tissue. However, in response to antigenic stimulus (i.e. H Pylori), normally present T cells in the gastric mucosa attract a B cell population, to give rise to lymphoid follicles. With prolonged simulation, lymphomas. Other sites are possible (orbit, parotid, small bowel), but with less frequency compared with the stomach.
151. In single fraction SBRT to the pancreas using doses of 25 Gy x 1, what was the dose limiting organ?
   a. Common bile duct
   b. Duodenum
   c. Liver
   d. Kidney

Key: B
Rationale: In Murphy et al, the median time to Grade 2-4 duodenal toxicity was 6.3 months (range, 1.6-11.8 months). The 6- and 12-month actuarial rates of toxicity were 11% and 29%, respectively. V(10)-V(25) and D(max) all correlated significantly with duodenal toxicity (p<0.05). In particular, V(15)>9.1 cm(3) and V(15)<9.1 cm(3) yielded duodenal toxicity rates of 52% and 11%, respectively (p=0.002); V(20)>3.3 cm(3) and V(20)<3.3 cm(3) gave toxicity rates of 52% and 11%, respectively (p=0.002); and D(max)>23 Gy and D(max)<23 Gy gave toxicity rates of 49% and 12%, respectively (p=0.004).

152. How is photon beam flatness characterized?
   a. The central 80% of the beam at a depth of dmax
   b. The central 50% of the beam at a depth of dmax
   c. The central 80% of the beam at a depth of 10 cm
   d. The central 50% of the beam at a depth of 10 cm

Key: C
Rationale: Beam flatness is defined at a depth of 10 cm of water using 80% of the central field dimension.

153. The rationale for modifying ABVD backbone, when integrating Brentuximab Vedotin is to reduce the risk of:
   a. neuropathy by omitting Vinblastine.
   b. cardiotoxicity by omitting adriamycin.
   c. pneumonitis by omitting Bleomycin.
   d. hematologic toxicity by omitting dacarbazine.

Key: C
Rationale: Brentuximab Vedotin + AVD is a safe regimen per the clinical trial and several others that are soon to be published.

154. What is the MOST acceptable radiation volume for a 6 year old boy with a localized grade III ependymoma in the 4th ventricle after gross total resection?
   a. No radiation
   b. Resection bed plus margin
   c. Whole ventricle and resection bed boost
   d. Craniospinal axis and resection bed boost

Key: B
Rationale: All patients over 12 months with intracranial grade II or grade II ependymoma should undergo adjuvant radiation therapy to the resection bed to 54 to 59.4 Gy. (There is an ongoing trial to observe patients with gross total resection of supratentorial Grade II ependymoma.) There is no role for craniospinal irradiation in patients who do not have evidence of disseminated disease.
155. For a fixed field size, which statement regarding percent depth dose (PDD) or tissue maximum ratio (TMR) is true?
   a. PDD takes into account inverse square variations
   b. TMR takes into account inverse square variations
   c. PDD decreases as the source to surface distance (SSD) increases
   d. TMR decreases as the source to surface distance (SSD) increases

**Key:** A  
**Rationale:** The PDD takes account of both inverse square attenuation and attenuation by the presence of matter. TMR accounts only for attenuation by the presence of matter and is therefore independent of distance. The value of the PDD increases as SSD increases.  

156. After completion of concurrent chemoRT with weekly paclitaxel (45-50 mg/m²) and carboplatin (AUC 2) for unresectable, stage III NSCLC, the next step is:
   a. PCI.
   b. consolidation durvalumab (10 mg/kg) every 2 weeks for 12 months.
   c. 2 cycles of paclitaxel (200 mg/m²) and carboplatin (AUC 6).
   d. consolidation nivolumab (3 mg/kg) every 2 weeks for 12 months

**Key:** NOTE: This item was multi-keyed for scoring purposes upon post-exam statistical item analysis (Both B and C were given credit as correct responses).  
**Rationale:** It is not a standard of care to offer PCI for patients with stage III NSCLC after chemoradiation since randomized trials did not demonstrate a survival benefit. After completion of concurrent chemoRT with weekly paclitaxel (45-50 mg/m²) and carboplatin (AUC 2) the next step is consolidation 2 cycles of paclitaxel (200 mg/m²) and carboplatin (AUC 6). Once this therapy is completed, based on the results from the recently published phase-III randomized trial (Antonia et al, NEJM 2017), patients with PS 0-1 and no disease progression can be treated with durvalumab (anti-PD L1 antibody) (10 mg/kg) every 2 weeks for 12 months or until progression. Consolidation nivolumab or pembrolizumab is not currently recommended for non-metastatic advanced NSCLC after completion of chemoRT.  

157. On COG 0031, a study of risk-adapted radiation in intermediate risk pediatric Hodgkin’s lymphoma, what was the MOST common location of relapse?
   a. Initial non-bulky sites of disease
   b. Initial bulky sites of disease
   c. Initial non-bulky and bulky sites of disease
   d. Outside the initial volume of disease

**Key:** C  
**Rationale:** Patients were equally likely to relapse in (74%) bulky and (75%) non-bulky sites of initial disease. 94% of relapses were within initial sites of disease involvement.  
158. Which is approved to reduce the effects of a radiation disaster?
   a. Pembrolizumab
   b. Amifostine
   c. MESNA
   d. Potassium iodide

Key: D

Rationale: Amifostine has been studied for the prevention of radiation mucositis but not as a mitigator; MESNA is used in reduce the incidence of hemorrhagic cystitis following ifosfamide or cyclophosphamide treatment; pembrolizumab is an immune checkpoint inhibitor; none of these compound is approved for use in a radiation emergency. Potassium iodide was approved by the FDA for use in the prevention of thyroid complications following an exposure to radioactive iodine.


159. A 1.5 cm diameter tumor composed of 108 clonogens is treated with conventional 2Gy/Fx regimen. The effective dose response curve is exponential with an effective D10 of 7Gy. Assume no cellular proliferation between fractions. What total dose corresponds to the TCD90 (90% probability of tumor control)?
   a. 45 Gy
   b. 54 Gy
   c. 63 Gy
   d. 72 Gy

Key: D

Rationale: Since the goal is to achieve a 90% tumor control rate, the total dose of radiation that is administered to the tumor should reduce the number of surviving clonogenic cells to an average of 0.1, or 10^-1. This is determined based on the equation P=e^(-N)(SF), where SF is the surviving fraction following the irradiation protocol, N is the initial number of clonogenic tumor cells, and P is the probability of tumor cure (0.9 or 90% in the present example). Therefore, since there were initially 108 clonogenic cells, in order to achieve a 90% control rate, the total radiation dose should reduce the surviving fraction to 10^-9, as this results in an average of 0.1 clonogens surviving in each tumor or that 1 cell survives out of every 10 tumors that is irradiated. Thus, as in the present case the survival curve is exponential with a D10 of 7Gy, a dose of 63 Gy would be required. D10 =7Gy For nine decades of cell kill 9x7 Gy = 63 Gy.


160. Where is Meckel’s cave, or the trigeminal cistern, located?
   a. A Lateral to the mesial temporal lobe
   b. B Superior to the level of the chiasm
   c. C Posterior to the internal auditory canal
   d. D Lateral to the cavernous sinus

Key: D

Rationale: Meckel’s cave, also known as the trigeminal cistern, trigeminal cave, or cavum trigeminale, is a CSF filled evagination containing the trigeminal ganglion, bounded laterally by the dura of the tentorium at the mesial temporal lobe, medially by the wall of the cavernous sinus, and inferiorly by the clivus and petrous bone.

161. Concerning pleomorphic lobular carcinoma in situ:
   a. mammographic identification is by architectural distortion.
   b. demonstrates central necrosis and calcification.
   c. surgical excision is not required.
   d. radiation therapy is indicated after breast conserving surgery.

**Key:** B

**Rationale:** Pleomorphic lobular carcinoma is a histologic variant of invasive lobular carcinoma that is associated with a poor prognosis. Pleomorphic LCIS has similar features to standard LCIS except for the finding of central necrosis with calcifications. It is associated with development of pleomorphic lobular carcinoma. There is no distinct mammographic appearance for pleomorphic LCIS. Management recommendation for pleomorphic LCIS is complete surgical excision with negative surgical margins.

**References:**

162. Which is NOT a recognized hallmark of cancer?
   a. Self-sufficiency in growth signals
   b. Activation of apoptosis
   c. Evading the immune system
   d. Limitless replicative potential

**Key:** B

**Rationale:** The original hallmarks of cancer were (1) self-sufficiency in growth signals; (2) insensitivity to anti-growth signals; (3) evading apoptosis; (4) limitless replicative potential; (5) sustained angiogenesis; (6) tissue invasion and metastasis. Four new hallmarks were added in 2011 including (1) abnormal metabolic pathways, (2) evading the immune system, (3) genome instability, and (4) inflammation. Tumors generally resist programmed cell death by evading apoptosis rather than activating apoptosis.

**References:**

163. According to the International Neuroblastoma Staging System, what is the stage of an 8 month old boy with an unresectable abdominal neuroblastoma crossing midline with a metastasis in the femoral bone?
   a. 2B
   b. 3
   c. 4
   d. 4S

**Key:** D

**Rationale:** For stage 4S, patients must be less than one year of age and have a localized tumor with dissemination limited to the skin, liver, and/or bone marrow. Metastasis to the bone is stage 4. An unresectable neuroblastoma crossing midline without metastasis is stage 3.

**References:**
164. What is the conclusion for a significance test with a p-value of 0.184 at a predetermined 0.10 level of significance?
   a. Accept null hypothesis
   b. Accept alternative hypothesis
   c. Fail to reject alternative hypothesis
   d. Fail to reject null hypothesis

**Key:** D  
**Rationale:** Use the rule: p-value < alpha, reject H0. The P-value is greater than the significance level α (=0.10), so we can conclude the data do not provide sufficient evidence to reject the null hypothesis (H0). Fail to reject H0.

165. According to GOG 33 (Creasman et al), what is the estimated risk of pelvic lymph node metastases for FIGO grade I adenocarcinoma of the endometrium, invading the deep third of the myometrium?
   a. 3 %
   b. 10 %
   c. 20 %
   d. 30 %

**Key:** B  
**Rationale:** Results of GOG33 may be used to estimate probability of nodal dissemination in endometrial cancer, complimented by more modern studies.  
**References:** Creasman WT, Cancer 1987 Oct 15, 60(8 Suppl):2035-41.

166. In breast cancer, which lymph nodes lay medial to the medial margin of the pectoralis minor muscle and portend a worse prognosis?
   a. Rotter’s nodes
   b. Level III Nodes
   c. Level I Nodes
   d. Internal mammary nodes

**Key:** B  
**Rationale:** The correct answer is B. The nodes that lay medial to the medial margin of the pectoralis minor muscle and inferior to the clavicle are level III nodes, also known as apical or infraclavicular nodes. When an individual is noted to have metastases in these nodes it confers a worse prognosis. The internal mammary nodes are located in the intercostal spaces along the edge of the sternum in the endothoracic fascia. Rotter’s nodes are interpectoral. Level I nodes are in the low axilla and are lateral to the lateral border of the pectoralis minor muscle.  
RTOG Breast Cancer Contouring Atlas.
167. Which is the appropriate treatment for T2N0 squamous cell carcinoma of the anal canal?
   a. Wide Local Excision
   b. Definitive chemoRT with 5FU/mitomycin C
   c. Neoadjuvant chemoRT followed by abdominoperineal resection
   d. Induction 5FU/Cisplatin followed by definitive chemoRT with 5-FU/cisplatin

**Key:** B

**Rationale:** A T1N0 well differentiated anal margin cancer may be treated with local excision with adequate margins. However, all poorly differentiated or T2 or N+ anal margin cancers require chemoradiation, as the adequate margins will require violation of the anal sphincter, potentially compromising sphincter function. Any N+ anal cancer patient should receive >45 Gy. In RTOG 98-11, these patients received 55-59 Gy with 3D conformal technique. In RTOG 0529, these patients received 54 Gy to the primary tumor, with 50.4-54 Gy to the involved lymph node region.


168. The efficacy of Amifostine (WR-2721; Ethyol) as a normal tissue radioprotector was demonstrated in a RTOG phase III trial for patients with tumors in which anatomical site?
   a. Head and Neck
   b. Kidney
   c. Brain
   d. Breast

**Key:** A

**Rationale:** Amifostine is an accepted radioprotector but animal studies have demonstrated it does not cross the blood brain barrier. However, in a series of clinical trials from multiple centres efficacy was shown in preservation of normal tissue for patients treated with head and neck cancers. Amifostine and its active metabolite, WR-1065, accumulate in many epithelial tissues with the highest concentrations found in the salivary glands and kidneys. Its putative mechanism of radioprotection is through the scavenging of radiation-induced free radicals. Small clinical trials have suggested that amifostine protects against radiation-induced xerostomia and mucositis. In patients with previously untreated head and neck squamous cell carcinoma using primary end points of incidence of grade > 2 acute xerostomia, grade > 3 acute mucositis, and grade > 2 late xerostomia. Amifostine administered (200 mg/m2 intravenous) daily 15 to 30 minutes before irradiation. Radiotherapy was given once daily (1.8 to2.0 Gy) to doses of 50 to 70 Gy. Amifostine reduced grade > 2 acute xerostomia from 78% to 51% (P < .0001) and chronic xerostomia grade > 2 from 57% to 34% (P 5 .002). Antitumor treatment efficacy was preserved. J Clin Oncol. 2000 Oct 1;18(19):3339-45.

**References:** Yuhas JM, Afzal SM, Afzal V; Variation in normal tissue responsiveness to WR-2721; Int J Radiat Oncol Biol Phys. Sep;10(9), 1984; 1537-1539.
Andreassen CN, Grau C, Lindegaard JC.; R Chemical radioprotection: a critical review of amifostine as a cytoprotector in radiotherapy; Semin Radiat Oncol. 2003 Jan; 13(1), 62-72.
169. A case-control study design:
   a. makes it easy to study diseases that have a long latency.
   b. may require long observational period to detect the disease.
   c. allows for multiple outcomes to be studied.
   d. requires disease-free groups at study initiation.

Key: A

Rationale: The case-control study design compares those with a disease of interest to those without. As such, it doesn’t require a long latency to detect the disease and doesn’t include disease-free groups at initiation. Also the study outcome is determined at outset, so multiple outcomes cannot be studied.


170. In patients with nasopharyngeal carcinoma, high pre-treatment plasma EBV DNA (>1500 copies/mL) is associated with:
   a. improved OS.
   b. worse OS.
   c. decreased acute toxicity.
   d. increased acute toxicity.

Key: B


Rationale: Overall survival and relapse-free survival were significantly lower among patients with elevated (at least 1500 copies per millilitre) pre-treatment EBV DNA concentrations compared with patients with <1500 copies per millilitre.

171. Which predicts higher incidence of vertebral compression fractures after spinal SBRT?
   a. Radiation dose ≥ 20 Gy in a single fraction
   b. Radiation resistant tumor histology (e.g. renal, melanoma)
   c. Male gender
   d. Blastic tumors

Key: A

Rationale: Increased risk for vertebral compression fracture (VCF) was associated with dose > 20 Gy in a single fracture, lytic lesions, prior VCF, female gender, primary hematologic malignancies, thoracic spine lesions, and spinal deformity in these series.

Sahgal, A. et. al., Vertebral Compression Fractures After SBR: Multi-institutional Analysis with Focus on Spinal Dose and Spinal Instability Neoplastic Score. JCO 2013; 31: 3426.
172. Which of these agents is commonly used as a radiosensitizer?
   a. Avastin
   b. Tirapazamine
   c. Cisplatin
   d. Adriamycin

**Key:** C  
**Rationale:** Concurrent administration of radiation and chemotherapy has emerged as a dominant form of cancer treatment. Nevertheless, our understanding of the specific mechanisms of interaction between radiation and chemotherapy is still evolving. Biological evidence gained in experimental cell lines and tumors suggests that cisplatin lesions cause repair inhibition of radiation-induced DNA damage affecting both homologous recombination and nonhomologous end joining and therefore act as a radiosensitizer.  
**References:** Wilson GD, Bentzen SM, Harari PM., Biologic basis for combining drugs with radiation, Semin Radiat Oncol. 2006 Jan;16(1);2-9.

173. Rotating anodes are used in many diagnostic X-ray tubes because the rotation:
   a. allows for increased image contrast.  
   b. offers better heat dissipation.  
   c. creates a flat x-ray beam.  
   d. allows for higher image resolution.

**Key:** B  
**Rationale:** A rotating anode reduces the temperature at the target at any one point.  

174. For the purpose of reporting dose statistics, when a primary planning target volume (PTV) overlaps a planning organ at risk volume (PRV):
   a. the PTV should be trimmed back to avoid the PRV.
   b. the PRV should be trimmed back to avoid the PTV.
   c. neither the PTV or PRV should be changed.
   d. both the PRV and PTV should be modified as a compromise.

**Key:** C  
**Rationale:** “To ensure accurate reporting of absorbed dose to the PTV in cases for which the PTV encroaches or overlaps another PTV, OAR or PRV, it is now recommended that the delineation of the Primary PTV margins should not be compromised” Additional volumes may be created (for optimization purposes only) in which the PTV is trimmed to avoid the OAR.  

175. A medically inoperable patient with endometrial cancer has disease confined to the uterus by MRI. When is treatment using only brachytherapy MOST appropriate?
   a. Uterine serous carcinoma with >50% of myometrial invasion  
   b. FIGO grade 1 adenocarcinoma with <50% myometrial invasion  
   c. Uterine serous carcinoma with < 50% myometrial invasion  
   d. FIGO grade 3 endometrioid adenocarcinoma with > 50% myometrial invasion

**Key:** B  
**Rationale:** Intracavitary brachytherapy, with implants placed into the uterine cavity, is an effective definitive treatment for endometrial cancer. Brachytherapy alone does not adequately treat adnexa or pelvic lymph nodes. Therefore, addition of EBRT is advised when tumor characteristics suggest elevated risk of subclinical cancer spread beyond corpus uteri, as in other scenarios listed here.  
176. What is the most common histology of intramedullary spinal cord tumors in adults?
   a. Meningioma
   b. Ependymoma
   c. Astrocytoma
   d. Lymphoma

   **Key:** B
   **Rationale:** Meningioma is the most common spinal tumor in adults but occurs in the intradural-extradural space. Ependymoma is the most common intramedullary tumor.

177. What is the line that extends from the medial canthus of the eye to the angle of the mandible?
   a. Pupillary line
   b. Ohngren’s line
   c. Zygomatic line
   d. Reid’s line

   **Key:** B
   **Rationale:** Ohngren’s line divides the maxillary sinus into an anterior-inferior part, and a superior-posterior part. Tumors that arise below Ohngren’s line have a better prognosis.
   **References:** Cox, James D., MD; Ang, K. Kian, MD, PhD, Radiation Oncology: Rationale, Technique, Results, 2010, Mosby, 9th, 183-206.

178. Regarding the German Hodgkin Study Group HD11 trial:
   a. both IFRT and ISRT were permitted.
   b. PET imaging was not utilized for staging or assessing treatment response.
   c. there was no significant difference in disease control between 20 Gy and 30 Gy.
   d. BEACOPP resulted in significantly less toxicity than ABVD.

   **Key:** B
   **Rationale:** The GHSG HD11 trial in early stage unfavorable Hodgkin lymphoma patients did not utilize PET scan. Although 20 Gy was not inferior to 30 Gy after BEACOPP, inferiority of 20 Gy could not be excluded after ABVD. BEACOPP resulted in more toxicity than ABVD. Involved field radiation therapy was the only permitted technique.

179. Which of the following was NOT a treatment arm on the UK IMPORT LOW trial for early stage breast cancer patients treated with breast conservation?
   a. 40 Gy/15 fx partial breast
   b. 36 Gy/15 fx whole breast and 40 Gy/15 fx to partial breast
   c. 40 Gy/15 fx whole breast
   d. 40 Gy/15 fx whole breast and 48 Gy/15 fx boost

   **Key:** D
   **Rationale:** The 3 arms of the UK IMPORT LOW study were 40 Gy/15 fx whole breast (control group); 36 Gy/15 fx whole breast and 40 Gy/15 fx to partial breast (reduced dose group); 40 Gy/15 fx partial breast (partial breast group). 5 year results from this RCT showed noninferiority of the reduced dose and partial breast groups compared to the whole breast control group for local control and normal tissue adverse effects. Option D is the experimental arm on RTOG 1005 with concurrent boost to 48 Gy.
   **References:** Lancet Coles CE et al 2017:390, 1048-1060.
180. What was the prescription dose in the multi-institutional phase II study of SBRT for locally advanced pancreatic cancer (Herman, et. al. 2015)?
   a. 8 Gy x 3
   b. 26 Gy x 1
   c. 6.6 Gy x 5
   d. 15 Gy x 3

Key: C
Rationale: The study treated 49 patients with gemcitabine followed by SBRT (6.6 Gy x 5) and then additional gemcitabine. The median overall survival was 13.9 months. The grade 2+ acute toxicity rate was 2%. The grade 2+ late toxicity rate was 11%. The prescription of 15 Gy x 3 was used by Hoyer et al, and found to be unacceptably toxic.

181. A patient presents with epistaxis and the MRI findings below. Pathology shows small cells, positive for synaptophysin, chromogranin, and epithelial markers. Melanoma markers were negative. What is the MOST likely diagnosis?
   a. Benign pansinusitis
   b. Adenocarcinoma of the nasal cavity
   c. SCC of the nasal cavity
   d. Esthesioneuroblastoma of the nasal cavity

Key: D
Rationale: The provided image represents a case of newly diagnosed, advanced esthesioneuroblastoma with intracranial extension but without regional nodal or distant metastatic spread. This uncommon tumor is associated with improved prognosis with respect to other paranasal sinus malignancies, particularly SNUC. Synaptophysin and chromogranin markers indicate neuroendocrine tumors and would exclude adenocarcinoma and squamous cell carcinoma which can also occur in this area. Absence of melanoma markers excludes melanoma which may also be found at this site.

182. What is the optimal radiation linear energy transfer (LET) to obtain the highest relative biological effectiveness (RBE) for DNA double strand breaks production?
   a. 1 keV/mm
   b. 10 keV/mm
   c. 100 keV/mm
   d. 1000 keV/mm

Key: C
Rationale: RBE remains relatively constant as the LET increases from 1 keV to 10 KeV. The largest change in RBE with increasing LET is over the LET range of 10-100 keV/uM, with the largest RBE seen at 100 keV. The RBE decreases as the LET increases from 100 keV/uM to 1000 keV/uM. At 100 keV/uM the distribution and deposition of ionizing events is optimal to cause breaks on both strands of DNA.
183. In the Stockholm III trial for rectal cancer, what were the three arms to which patients were randomized?
   a. Radiation (50 Gy) with delay to surgery; short course radiation (25 Gy) with delay to surgery; short course radiation (25 Gy) without delay to surgery
   b. ChemoRT (50 Gy + 5-FU) with delay; short course radiation (25 Gy) with delay to surgery; short course radiation (25 Gy) without delay to surgery
   c. ChemoRT (50 Gy + capecitabine) with delay to surgery; ChemoRT (50 Gy+ capecitabine) without delay to surgery; short course radiation (25 Gy) with delay to surgery
   d. ChemoRT (50 Gy + capecitabine) with delay to surgery; ChemoRT (50 Gy+ capecitabine) without delay to surgery; short course radiation (25 Gy) without delay to surgery

Key: A  

Rationale: In this study, participants were randomly assigned with permuted blocks, stratified by participating centre, to receive either $5 \times 5$ Gy radiation dose with surgery within 1 week (short-course radiotherapy) or after 4-8 weeks (short-course radiotherapy with delay) or $25 \times 2$ Gy radiation dose with surgery after 4-8 weeks (long-course radiotherapy with delay). Delaying surgery after short-course radiotherapy gives similar oncological results compared with short-course radiotherapy with immediate surgery. Long-course radiotherapy with delay is similar to both short-course radiotherapy regimens, but prolongs the treatment time substantially. Although radiation-induced toxicity was seen after short-course radiotherapy with delay, postoperative complications were significantly reduced compared with short-course radiotherapy.


184. Which treatment is appropriate adjuvant therapy for resected pancreatic cancer?
   a. Gemcitabine followed by gemcitabine-based ChemoRT
   b. FOLFIRINOX followed by FOLFIRINOX-based ChemoRT
   c. Gemcitabine/capecitabine followed by gemcitabine/capecitabine based ChemoRT
   d. 5FU followed by 5FU based ChemoRT

Key: D  

Rationale: 5FU or capecitabine-based chemoradiation are the only standard-of-care options for adjuvant chemoradiation in pancreatic cancer. RTOG 9704 tested gemcitabine vs 5FU chemotherapy as adjuvant therapy, but all pts received their chemoRT with 5FU because of toxicity concerns with large adjuvant treatment volumes and gemcitabine. Gemcitabine alone was supported by the CONKO-001 study. No radiation was given on this trial. The ESPAC-4 study has demonstrated superiority of gemcitabine and capecitabine over gemcitabine alone in the adjuvant setting. No radiation was given on this trial. Concurrent gemcitabine and radiation should be reserved for situations with smaller treatment volumes (such as neoadjuvant, or definitive/palliative CRT) in order to minimize the GI toxicity of chemoradiation.

A new screening test for a certain disease is being evaluated. The table below shows the frequencies by the true disease status and screening test result.

<table>
<thead>
<tr>
<th>Screening Test Result</th>
<th>True Disease Status</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>Positive</td>
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<td>Negative</td>
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What is the sensitivity of a screening test?

a. \( \frac{a}{a+c} \)

b. \( \frac{d}{b+d} \)

c. \( \frac{a}{a+b} \)

d. \( \frac{d}{c+d} \)

**Key:** A  **NOTE:** This item was 0-weighted for scoring purposes upon post-exam statistical item analysis (did not count for or against candidate in calculation of test scores), because the table was missing in some of the printed test booklets.

**Rationale:** Screening refers to the application of test to people who as yet have no symptoms of a particular disease. It is classified as having a positive (disease likely) or negative (disease unlikely) finding. Diagnostic tests tell whether or not a subject actually has the disease. The performance of a screen test is considered by the sensitivity and specificity. The sensitivity is the percentage of subjects with disease who are classified as having disease and the specificity is the percentage of subjects without disease who are classified as not having disease. Those subjects with the disease should all be classified as having disease, and those subjects without the disease should be classified as not having disease. Therefore, a highly sensitive and specific test is preferred.


The quality of an x-ray radiation beam is best described by:

a. surface dose.

b. PDD.

c. dmax.

d. biological effects.

**Key:** B  **Rationale:** An ideal way to describe the quality of an x-ray beam is to specify its energy fluence; however, it is difficult to measure. A simpler specification of beam quality is to determine the penetrability of an x-ray beam as denoted by the PDD10 (MV beams) or HVL (kV beams).

**References:** Khan. The Physics of Radiation Therapy. Lippincott Williams and Wilkins. 2003. 3rd Ed.
187. A patient with nasopharyngeal carcinoma is unable to abduct the right eye and has numbness on the right forehead, cheek and upper lip with normal sensation of the right chin and lower lip. These symptoms indicate tumor involvement of what structure?
   a. Foramen lacerum
   b. Meckel’s cave
   c. Foramen ovale
   d. Cavernous sinus

   **Key:** D

   **Rationale:** These symptoms indicate involvement of cranial nerve (CN) VI, CN V-1, and CN V-2. Involvement of CN-VI explains the inability to abduct the right eye. Numbness of the forehead and cheek/upper-lip indicate involvement of CN V-1 and CN V-2. The sensation on the lower face indicates sparing of CN V-3 which passes through the foramen ovale. Meckel’s cave contains the trigeminal ganglion from which emerge CN V-1, CN V-2, and CN V-3. CN VI, CN V-1, and CN V-2 all pass through the cavernous sinus. A lesion in the cavernous sinus would explain the listed deficits.


188. According to the ASTRO APBI consensus statements, which of the following is an exclusion criterion for partial breast radiation?
   a. Tumor necrosis
   b. Tumor size 2 cm
   c. Age 50 years
   d. pN1 disease

   **Key:** D

   **Rationale:** The original 2009 consensus statement has been updated. Positive lymph nodes remain an exclusion criterion.

   **References:** Smith, B.D. et. al. IJROBP. 2009; 74(4)987.

189. Recognizing to limit the dose to the rectum and sigmoid as much as feasible, what is the HIGHEST D2cc (EQD2) dose limit recommended per the ABS HDR guidelines for locally advanced cervical cancer?
   a. 80 Gy
   b. 75 Gy
   c. 65 Gy
   d. 60 Gy

   **Key:** NOTE: This item was 0-weighted for scoring purposes upon post-exam statistical item analysis (did not count for or against candidate in calculation of test scores).

   **Rationale:** The correct answer is A. Both the sigmoid and rectum are organs at risk which need to be addressed at the time of each brachytherapy implant. While doses of <60 and < 65 are excellent, they are lower and would achieve less toxicity. A dose limit of up to 80 Gy is too high and can result in injury to the rectum and sigmoid.

190. In the NCIC/EORTC randomized trial of glioblastoma patients > 65 years, what resulted from the addition of concurrent and adjuvant temozolomide to 40 Gy in 15 fractions?
   a. Improved OS
   b. Worsened OS
   c. Improved QoL
   d. Worsened QoL

Key: A
Rationale: The NCIC CE.6/EORTC 26062-22061 trial randomized 562 patients older than 65 years, with ECOG performance status 0-2, who were not deemed candidates for standard 60Gy with temozolomide (TMZ) chemotherapy, to: 40 Gy in 15 fractions alone vs. 40 Gy in 15 fractions with concurrent and adjuvant TMZ. The addition of TMZ improved OS (9.3 vs. 7.6 months) and PFS (5.3 vs. 3.9 months). Quality of life was similar in the two groups.

191. According to the GRECCAR-6 study evaluating optimal interval between neoadjuvant chemoradiotherapy and surgery for rectal cancer, compared to an 11 week interval, a 7 week interval:
   a. improved pCR rates.
   b. decreased pCR rates.
   c. had equivalent pCR, but higher postoperative morbidity.
   d. had equivalent pCR, but lower postoperative morbidity.

Key: D
Rationale: The primary end point (ypT0N0) was not different (7 weeks: 20 of 133, 15.0% v 11w: 23 of 132, 17.4%; P = .5983). Morbidity was significantly increased in the 11w group (44.5% v 32%; P = .0404) as a result of increased medical complications (32.8% v 19.2%; P = .0137). The 11w group had a worse quality of mesorectal resection (complete mesorectum [I] 78.7% v 90%; P = .0156). Waiting 11 weeks after RCT did not increase the rate of pCR after surgical resection. A longer waiting period may be associated with higher morbidity and more difficult surgical resection.

192. What occurs if a true null hypothesis is rejected, or if a difference is concluded when no difference exists?
   a. Type I error
   b. Type II error
   c. Nonstandard error
   d. Standard error

Key: A
Rationale: A Type I error results if a true null hypothesis is rejected or if a difference is concluded when no difference exists.
Cancer stem cells are important targets of anti-cancer treatment due to their role in:
   a. repair of normal tissue damage.
   b. the development of secondary cancers.
   c. cancer recurrence and therapeutic resistance.
   d. radiation recall reactions.

Key: C
Rationale: Cancer stem cells are pluripotent cells with high replicative potential, resistance to therapy, and ability to repopulate an entire tumor through differentiation. They are thought to be responsible for metastases and may be increased in sites of metastatic disease.

Which can be accelerated in a synchrotron?
   a. Gamma ray
   b. Neutron
   c. Deuteron
   d. Pion (π0)

Key: C
Rationale: In order for particles to be accelerated in a synchrotron, the particle must be charged. All of the listed particles are charge neutral except for the deuteron.

When compared to SPECT imaging, PET imaging possesses improved spatial resolution primarily because of:
   a. collimation.
   b. annihilation coincidence detection.
   c. filtered back projection.
   d. lower photon energy.

Key: B
Rationale: There is no difference between SPECT and PET for A, C, and D.

Which of the following target materials is most efficient at bremsstrahlung X-ray production?
   a. Aluminum
   b. Iron
   c. Copper
   d. Tungsten

Key: D
Rationale: X-ray production efficiency Z*V. With the same voltage, the higher atomic number, the more efficient.
References: Khan FM. The Physics of Radiation Therapy. Lippincott Williams and Wilkins. 2003, p. 34. 3rd Ed.
According to the EORTC/LYSA/GELA H10F study, PFS for patients with favorable early stage Hodgkin lymphoma who were interim PET negative, was:

a. superior with combined modality compared with ABVD alone.
b. inferior with combined modality compared with ABVD alone.
c. similar with combined modality compared with ABVD alone.
d. similar compared with PET positive patients treated with ABVD + INRT.

Key: A

Rationale: Combined modality therapy was associated with significant improvement over chemo alone for interim PET neg patients. Patients who were interim PET positive and received ABVD +INRT had inferior PFS than those who were PET negative.


How would the AJCC 7th and 8th editions of TNM staging system characterize T4malignant pleural mesothelioma?

a. Involvement of the endothoracic fascia
b. Focal extension into the soft tissues of the chest wall
c. Non-transmural involvement of the pericardium
d. Direct extension of tumor to the contralateral pleura

Key: D

Rationale: The definitions of T3 and T4 tumors did not change between the 7th and 8th editions. T3 tumors are those that are locally advanced but technically resectable. T4 tumors are technically unresectable. The T staging factors that render a tumor unresectable (T4) are diffuse extension or multifocal masses of tumor in the chest wall with or without associated rib destruction, direct trans-diaphragmatic extension of tumor to the peritoneum, or contralateral pleura, or mediastinal organs, or spine or tumor extending through to the internal surface of the pericardium with or without a pericardial effusion or tumor involving the myocardium.


Multiple myeloma:

a. arises from malignant transformation of T cells.
b. does not include MGUS or plasma cell leukemia.
c. has continued to rise in incidence since 1970s.
d. involves alteration in immunoglobulin heavy chain.

Key: NOTE: This item was 0-weighted for scoring purposes upon post-exam statistical item analysis (did not count for or against candidate in calculation of test scores).

Rationale: Multiple Myeloma is a disease spectrum that includes MGUS, plasma cell leukemia, as well as asymptomatic/smoldering, and symptomatic myeloma. It arises from the malignant transformation of B cells. The trends from 1970s-1990s showed increasing incidence, but a downward trend from 1992-2002; One of the earliest genetic events is the illegitimate switch recombination of partner oncogenes into the immunoglobulin heavy (IgH) chain. Other events may also occur.

200. Which is a microwave generator?
   a. Circulator
   b. Klystron
   c. Magnetron
   d. Thyratron

**Key:** C

**Rationale:** A magnetron generates microwaves by accelerating electrons across conductive gaps, inducing a resonant electromagnetic wave (microwave) that propagates out from the device. While similar in purpose, microwaves emitted from a klystron are the result of amplification of a low-power microwave source. A circulator diverts microwave power to prevent upstream reflection and maintain stability in a microwave transmission system. A thyratron is a high-energy switch used to create pulses of power.


201. Which sub-category of head and neck cancer has a new TNM staging system introduced in AJCC 8th edition?
   a. Lip
   b. Esthesioneuroblastoma
   c. Salivary gland
   d. Unknown primary

**Key:** NOTE: This item was multi-keyed for scoring purposes upon post-exam statistical item analysis (Both A and D were given credit as correct responses).

**Rationale:** New TNM staging systems have been added to the AJCC 8th edition for unknown primary, p16 positive oropharyngeal cancer, and head and neck sarcoma. Some lip cancers are staged as head and neck skin cancers which also has a new staging system, so lip is also included as an answer.


202. Which is the MOST appropriate MR imaging study to delineate a meningioma for SRS?
   a. T1
   b. T1 post contrast
   c. T2
   d. T2 FLAIR

**Key:** B

**Rationale:** A T1-post contrast scan is most appropriate as the meningioma will uptake the contrast. This will serve to provide a clear enhancement of the target volume in a T1 sequence.

**References:** Khan. The Physics of Radiation Therapy. Lippincott Williams and Wilkins. 2003. 3rd Ed.
203. What is the recommended treatment in limited-stage-SCLC based on the phase III randomized study (CONVERT) of concurrent chemoRT with once-daily RT to 66 Gy vs. twice-daily RT to 45 Gy?
   a. Twice-daily RT, due to improved efficacy over once-daily RT
   b. Once-daily RT, due to improved efficacy over twice-daily RT
   c. Once-daily RT, due to improved toxicity over twice-daily RT
   d. Twice-daily RT, due to lack of superiority of once-daily RT

Key: D
Rationale: The CONVERT trial was designed to examine superiority of once-daily vs. twice daily RT, and at a median follow-up of 45 months, median overall survival was 30 months (95% CI 24–34) in the twice-daily group versus 25 months (21–31) in the once-daily group (HR in the once daily group 1.18 [95% CI 0·95–1·45]; p=0·14). Survival and toxicity did not differ, but since the trial was designed to show superiority of once-daily RT and not powered for equivalence, authors recommend twice-daily RT to be considered standard of care.

204. A fixed effects model is most appropriate in a meta-analysis when study findings:
   a. are homogenous.
   b. are heterogenous.
   c. either homogenous or heterogenous.
   d. neither homogenous or heterogenous.

Key: A
Rationale: Fixed effects models consider only within-study variability. The assumption is that studies use identical methods, patients and measurements; that they should produce identical results; and that differences are only due to within-study variation. If studies are homogenous, researchers should use a fixed effects model.

205. What is the T stage for an upper tract urothelial carcinoma with invasion into the muscularis?
   a. T1
   b. T2
   c. T3
   d. T4

Key: B
Rationale: AJCC T staging for renal pelvic and upper tract urothelial cancers is based on depth of invasion. Invasion into the muscularis is considered T2 disease.

206. A beam arrangement where the distance from the source to the isocenter stays constant is referred to as the:
   a. SAD technique.
   b. SSD technique.
   c. SID technique.
   d. SPD technique.

Key: A
Rationale: In the SAD technique, the distance from the source to the isocenter is constant even if the distance to the skin changes.
207. Which cranial nerve provides tactile sensation for the anterior tongue?
   a. V
   b. VII
   c. IX
   d. XII

Key: A
Rationale: Cranial nerve V (lingual branch of V3) provides tactile sensation for the anterior 2/3 of the tongue, as well as pain, pressure, and temperature. Cranial nerve VII provides gustatory innervation for the anterior 2/3 of the tongue. Cranial nerve IX provides sensory and gustatory innervation for the posterior 1/3 of the tongue. Cranial nerve XII provides motor innervation of the tongue.

208. In the testes, what minimum dose range in 2 Gy fractions produces permanent sterility?
   a. 2-4 Gy
   b. 6-8 Gy
   c. 10-12 Gy
   d. 14-16 Gy

Key: B
Rationale: In humans, doses as low as 0.15 Gy was cause temporary sterility. Azoospermia for longer than 12 months can occur after a single dose of 2 Gy, with permanent azoospermia after 6 Gy-8 Gy delivered in 2 Gray fractions. Fractionation is more effective at killing stem cells in the testes because first dose stimulates radioresistance cells to move through the cell cycle into more radiosensitive phases which are killing by subsequent treatments. Likewise, azoospermia is sensitive to low dose rate treatments.

209. What is an appropriate initial drug/therapy to add to systemic chemotherapy or endocrine therapy in a patient with bone involvement in Stage IV breast cancer?
   a. Vitamin E
   b. Vitamin A
   c. Zoledronic acid
   d. Megestrol acetate

Key: C
Rationale: In patients with de novo or systemic stage IV breast cancer with bone involvement, NCCN guidelines recommend either denosumab, zoledronic acid, or pamidronate with calcium and Vitamin D supplementation. There is no recommendation for Vitamin E or Vitamin A. Megestrol acetate is one of the endocrine therapies utilized for Stage IV or recurrent disease.
210. The PARADIGM and DeCIDE trials tested induction chemotherapy followed by chemoRT vs concurrent chemoRT in locally advanced head and neck squamous cell carcinoma. What was the outcome of adding induction chemotherapy in these trials?
   a. Improved overall survival
   b. Increased toxicity
   c. Improved locoregional control
   d. Increased distant metastases

Key: B
Rationale: The PARADIGM and DeCIDE trials closed early due to poor accrual, however both of them declined to show an OS or PFS benefit to adding induction chemotherapy to chemoRT. Adding induction chemo increased severe toxicity and appeared to decrease the incidence of distant metastases in the DeCIDE trial.

211. In the retrospective review of NSCLC patients treated with definitive 3DCRT by Graham et al., which of the following factors was found to be the only predictor of Grade 2 or more radiation pneumonitis?
   a. Sequential or concurrent chemotherapy
   b. Mean lung dose
   c. Lung volume exceeding 20 Gy (V20)
   d. Location of the primary tumor (upper vs lower lobes)

Key: C
Rationale: In this retrospective review of 99 patients treated with definitive 3DCRT, the lung V20, Veff and mean dose, and location of primary tumor (upper vs lower lobe) predicted for Grade ≥2 radiation pneumonitis on univariate analysis. A lung V20 > 40% was associated with an actuarial incidence of Grade ≥ 2 pneumonitis of 36% while a lung V20 < 22% resulted in no incidences of Grade ≥2 pneumonitis. On multivariate analysis, only the lung V20 predicted for radiation pneumonitis (P=0.001).

212. What is the HDR brachytherapy target volume for inoperable Stage I adenocarcinoma of the endometrium?
   a. Uterus
   b. Uterus and cervix
   c. Uterus, cervix and upper 3-5 cm vagina
   d. Uterus, cervix and entire vagina

Key: C
Rationale: The target volume is the entire uterus, cervix, and upper 3-5 cm of vagina. The required length of the vagina to be treated cannot be encompassed by ovoids. The use of ovoids should be limited to cases with lower uterine segment involvement or Stage II disease where the medial parametrium is a part of the target volume.
213. In the randomized phase III CHECKMATE 025 clinical trial, how did nivolumab compare with everolimus for previously treated patients with advanced renal cell carcinoma?
   a. Significant improvement in OS
   b. Significant improvement in PFS
   c. Non-significant improvement in PFS
   d. No difference in grade 3 or 4 treatment-related toxicities

   Key: A
   Rationale: Everolimus, an mTOR inhibitor, is a recommended systemic therapy for advanced renal cell carcinoma that has failed other systemic treatments. It’s use, however, is still associated with limited overall survival. In a phase III open label randomized control trial, nivolumab resulted in a 5.4 month overall survival advantage over everolimus in previously treated patients (25 vs 19.6 months)

214. Specificity of a screen test is the percentage of subjects:
   a. without disease who are classified as having disease.
   b. with disease who are classified as not having disease.
   c. without disease who are classified as not having disease.
   d. with disease who are classified as having disease.

   Key: C
   Rationale: Screening refers to the application of test to people who as yet have no symptoms of a particular disease. It is classified as having a positive (disease likely) or negative (disease unlikely) finding. Diagnostic tests tell whether or not a subject actually has the disease. The performance of a screen test is considered by the sensitivity and specificity. The sensitivity is the percentage of subjects with disease who are classified as having disease and the specificity is the percentage of subjects without disease who are classified as not having disease. Those subjects with the disease should all be classified as having disease, and those subjects without the disease should be classified as not having disease. Therefore, a highly sensitive and specific test is preferred.

215. For a LDR brachytherapy implant for prostate cancer patient, which pre-implant parameter is consistent with good implant dosimetry?
   a. V100 > 90%
   b. D90>100%
   c. V150 >50%
   d. Rectal D0.1CC<200%

   Key: B
   Rationale: An ideal LDR prostate implant should have a D90 (the dose that covers 90% of the volume of the CTV) larger than the prescription dose (D90> 100% of prescription dose). As well, V100 (the percentage of the CTV that receives at least the prescribed dose) must be at least 95% (V100> 95% of CTV). The V150 (the percentage of the CTV that receives at least 150% of the prescription dose), should be equal to or less than 50% (V150\leq50\% of CTV). For the rectum, the D0.1cc should be < 150% of reference prescription dose
   References: AAPM Task Group 137, American Association of Physicists in Medicine, 2009.
216. What would be recommend for a 62 year old with FIGO IAG1 endometrioid adenocarcinoma of the endometrium after total hysterectomy without adverse risk factors?
   a. EBRT
   b. Observation
   c. Concurrent chemoRT
   d. Vaginal brachytherapy

Key: B
Rationale: Observation is preferred for low risk stage I endometrial cancer. In a randomized study by Sorbe et al, vaginal brachytherapy was compared to observation for women with IAG1 or IAG2 endometrioid adenocarcinoma. Fewer than 4% patients in the observation arm had vaginal or pelvic recurrence. The median age in the study was 62.7 years.

217. What is the radiation dose for testicular relapse of a patient with leukemia?
   a. 12 Gy
   b. 20 Gy
   c. 30 Gy
   d. 36 Gy

Key: NOTE: This item was multi-keyed for scoring purposes upon post-exam statistical item analysis (Both B and C were given credit as correct responses).
Rationale: 24 to 26 Gy over 2.5 to 3.5 weeks are considered historical standards. When, one testes is involved, imaging or biopsy of the contralateral testes frequently reveals contralateral disease. Thus, unilateral irradiation or orchiectomy as local management is associated with significant risk of contralateral testicular relapse. Recommendations are to treat both sides.

218. In a patient with NHL, what is a CONTRAINDICATION for receiving yttrium-90 ibritumomab tiuxetan?
   a. ≥25% lymphoma marrow involvement
   b. Platelet count >100,000 × 109/mL
   c. Body weight >70 kg
   d. Age >80 years

Key: A
Rationale: Because yttrium-90 ibritumomab tiuxetan can result in severe cytopenias, it is contraindicated if ≥25% lymphoma marrow involvement and if platelet count is <100,000 × 109/mL. While dosing is based on weight, there is no contraindication based on weight alone. Age has not been demonstrated to affect morbidity from yttrium-90 ibritumomab tiuxetan and thus is not a contraindication.

219. What is the FIGO stage for a cervical cancer with direct extension to the distal 1/3rd of the vagina and without parametrial invasion?
   a. IIA
   b. IIB
   c. IIIA
   d. IIIB

Key: C
Rationale: FIGO staging distal 1/3rd vagina extension is FIGO IIIA
220. What is the median, lethal single fraction radiation dose for TBI without hematopoietic stem cell rescue?
   a. 1 Gy
   b. 4 Gy
   c. 8 Gy
   d. 12 Gy

**Key:** B  
**Rationale:** The median single fraction TBI irradiation dose without stem cell rescue is 4 Gy.  

221. Which biologic subtype of breast cancer is associated with the lowest risk of in-breast recurrence at 5 years after breast-conserving therapy?
   a. ER/PR negative, Her2 negative
   b. ER/PR negative, Her2 positive
   c. ER/PR positive, Her2 negative
   d. ER/PR positive, Her2 positive

**Key:** C  
**Rationale:** Hattangadi-Gluth et al. reviewed the outcomes of 1223 women with T1-T2N0-N3 breast cancer treated with breast-conserving therapy between 1998 and 2003. The 5-year risk of in-breast recurrence were 9% for Her-2 type, 4.4% for triple negative, 1.2% for ER/PR+ H2N+, and 0.2% for ER/PR+, H2N-. Biologic subtype is clearly prognostic for in-breast recurrence, and the luminal A subtype – variably defined but typically ER/PR+, H2N-, grade 1-2 – appears to be the most favorable group with current therapeutic regimens. Of note, the advent of trastuzumab appears to have substantially reduced the risk of in-breast recurrence in the Her-2 type as compared to the series above.  

222. What is the approximate rate of distant metastases for FIGO stage IBG3 endometrioid adenocarcinoma treated with total hysterectomy and EBRT?
   a. 3%
   b. 10%
   c. 20%
   d. 30%

**Key:** D  
**Rationale:** Patients with deeply invasive, high grade endometrioid adenocarcinoma of the endometrium (2009 FIGO stage IBG3) are at high risk of distant relapse and carcinoma-related death. Several phase III studies evaluating the role of adjuvant chemotherapy for similar patients have recently completed accrual.  
**References:** Creutzberg CL, J Clin Oncol. 2004 Apr 1, 22(7): 1234-41.
223. The risk of dry eye syndrome is approximately 5% at a lacrimal gland dose of approximately:
   a. 10 - 20 Gy.
   b. 30 - 40 Gy.
   c. 50 - 60 Gy.
   d. 70 - 80 Gy.

Key: B
Rationale: Most data sets suggest a risk of dry eye syndrome of 5–10% at 30-40 Gy maximum dose to the lacrimal gland. Bhandare et al., modeled a 5% risk at 34 Gy and 10% risk at 38Gy. Based on similar data, Batth et al. suggested preliminary IMRT planning guidelines of 30 Gy maximum and 25 Gy mean lacrimal dose when achievable.

224. What is the consolidation radiation dose range for early stage mantle cell lymphoma?
   a. 20-24 Gy
   b. 30-36 Gy
   c. 40-45 Gy
   d. 50-54 Gy

Key: B
Rationale: 30-36 Gy is an acceptable radiation dose range.

225. What is the expected local control after radiation therapy for pituitary adenomas?
   a. 30%
   b. 50%
   c. 70%
   d. >90%

Key: D
Rationale: The local control for pituitary adenomas is greater than 90% with radiation therapy.

226. According to an EBCTCG meta-analysis, what is the effect of radiation following breast conserving surgery on 10 year recurrence and 15 year breast cancer mortality?
   a. One breast cancer death prevented for every 4 recurrences avoided
   b. One breast cancer death prevented for every 7 recurrences avoided
   c. Approximately 50% reduction in LR and no reduction in mortality
   d. Approximately 75% reduction in LR and 10% reduction in mortality

Key: A
Rationale: The EBCTCG meta-analysis of breast conserving surgery and radiation showed that RT reduced the 10-year risk of recurrence from 35.0% to 19.3% (absolute reduction 15.7%, 95% CI 13.7–17.7, 2p<0·00001) and reduced the 15-year risk of breast cancer death from 25.2% to 21.4% (absolute reduction 3.8%, 1.6–6.0, 2p=0·00005). Approximately one breast cancer death was avoided for every four recurrences prevented.
227. What is the most common histology of primary CNS lymphoma?
   a. Hodgkin lymphoma
   b. Burkitt lymphoma
   c. Follicular lymphoma
   d. Diffuse large B-cell lymphoma

Key: D
References: Hoang-Xuan, Lancet Oncology, July 2015, Hoang-Xuan, e322-32.
Rationale: Primary CNS lymphoma is a DLBCL. Other systemic lymphomas can secondarily involve the CNS.

228. After flank or whole abdomen radiation, when is supplemental boost irradiation indicated in Wilms tumor?
   a. Diffuse anaplasia
   b. Gross residual disease
   c. Preoperative tumor spill
   d. Resected positive lymph nodes

Key: B
Rationale: Supplemental boost irradiation following flank irradiation is required in patients with gross residual disease. In patients with diffuse anaplasia, the total dose following 10.8 Gy of supplemental boost irradiation is 30.6 Gy. In patients with favourable histology who have gross residual disease, the total dose is 21.6 Gy.
References: John Kalapurakal and Arnold Paulino AREN0534.

229. The inverse planning technique called multicriteria optimization (MCO) is best described as a technique that accounts for:
   a. multiple OARs constraints in the objective function.
   b. tissues heterogeneities in the optimization using Monte Carlos dose calculation methods.
   c. both multiple OARs and target volumes in the objective function.
   d. various objective functions during optimization.

Key: D
Rationale: The basic concept behind MCO is that one does not know which objective function should be employed. The use of MCO in practice allows planners to use various objective functions in conjunction with relative importance weights between OARs and target constraints.

230. A delta ray is:
   a. a high energy deuteron particle.
   b. a proton after elastic scattering with a neutron.
   c. an atomic electron ejected from an atom.
   d. an electron emitted by the nucleus.

Key: C
Rationale: A delta ray is an atomic electron ejected from an atom when bombarded by high energy electrons. An electron emitted by the nucleus is called a beta particle.
231. In the randomized Phase-II RTOG 0915 study comparing two SBRT schedules for medically inoperable patients with stage I peripheral NSCLC, the single fraction SBRT dose was:
   a. 21 Gy.
   b. 24 Gy.
   c. 30 Gy.
   d. 34 Gy.

**Key:** D  
**Rationale:** RTOG 0915 study randomized patients with medically inoperable, peripherally located, stage I NSCLC to receive either 34 Gy in 1 fraction or 48 Gy in 4 fraction. The incidence of grade 3 or more protocol-specified adverse events at 1 year were 10.3% and 13.3% respectively. At 1 year, primary tumor control rates were 97% and 92.7% respectively.  

232. Per the combined analysis of SOFT (Suppression of Ovarian Function) and TEXT (Tamoxifen and Exemestane) trials, which adjuvant endocrine therapy is recommended with GnRH agonist in high risk premenopausal ER positive breast cancer patients after completion of adjuvant chemotherapy?  
   a. Tamoxifen
   b. Anastrozole
   c. Exemestane
   d. Faslodex

**Key:** C  
**Rationale:** 5 year DFS in exemestane suppression group was 91% vs. 87% for tamoxifen group. 5 year FF breast cancer in exemestane ovarian suppression group was 93% vs. 89% in tamoxifen group.  
**References:** Pagani, D. et. al.,NEJM. 2014; 371(2). p. 107.

233. What is the 2-year local control rate of primary renal cancer treated with stereotactic radiation therapy?  
   a. 30%
   b. 50%
   c. 70%
   d. 90%

**Key:** D  
**Rationale:** Stereotactic body radiation therapy (SBRT) has been shown to provide good local control for primary renal cell carcinoma.  

234. Which criteria is used to define Active (symptomatic) Myeloma?  
   a. Hypocalcemia
   b. Anemia
   c. Hyponatremia
   d. Hypovolemia

**Key:** B  
**Rationale:** All of the above are part of the “CRAB” criteria use to determine symptomatic myeloma à C-Elevated Calcium, R-Renal Insufficiency, A-Anemia, Bone-lytic/osteopenic lesions.  
**References:** Durie BG et al. International response criteria for multiple myeloma, 2006, 1467-73.
235. What is an appropriate fractionated EBRT dose for a grade I meningioma recurrent after surgery?
   a. 14 Gy
   b. 36 Gy
   c. 54 Gy
   d. 60 Gy

Key: C
Rationale: Fractionated radiation doses range from 50 to 54Gy in 1.8’s to 2’s. RTOG 0539 used dose of 54Gy for intermediate risk meningiomas.

236. What is an ideal heart dose constraint for left sided breast cancers on the Alliance 11202 or NSABP B51 trials including regional nodal irradiation after neoadjuvant chemotherapy for cT1-3N0 breast cancers?
   a. V15 less than 50%
   b. V25 less than 15%
   c. Mean heart dose less than 4 Gy
   d. Maximal heart dose less than 35 Gy

Key: C
Rationale: For left sided treatment, the ideal heart dose constraints on Alliance 11202 and NSABP B-51 include: Mean Dose is less than 4 Gy, volume receiving more than 25 Gy (V25) is no more than 5% volume, and volume receiving more than 15 Gy (V15) is no more than 30% volume.
References: Heart Dose Constraints for breast cancer with regional nodal irradiation from the Alliance 11202 and NSABP B-51 trials.

237. What is the 20-year estimated risk of secondary breast cancer in women who received radiation therapy for Hodgkin lymphoma?
   a. .5%
   b. 19.5%
   c. 34.5%
   d. 49.5%

Key: A
Rationale: A retrospective study of 734 female Hodgkin lymphoma patients demonstrated that the 20-year estimate risk of secondary breast cancer was 7.5% after mantle field radiation therapy compared to 2.2% after chemotherapy only.

238. The soft palate is a subsite of which head and neck cancer site?
   a. Nasal cavity
   b. Maxillary sinus
   c. Oropharynx
   d. Oral cavity

Key: C
Rationale: The soft palate is part of the oropharynx. The superior surface of the soft palate creates part of the floor of the nasopharynx (which is not an option in the question)
References: Cox and Ang, Radiation Oncology, Editors, 2010, Mosby, 9th, 224-249.
239. What was the conclusion of the RICOVER RT-60 Trial for DLBCL?
   a. Patients < 60 yrs. benefited from addition of RT
   b. Patients with < 7.5 cm disease benefited from addition of RT
   c. RT (in per protocol analysis) improved EFS, PFS, and OS
   d. No benefit to added radiation

Key: C
Rationale: RICOVER RT 60 was designed to look at the benefit of RT after R-CHOPx6+2R for elderly patients between 61-80 with initial bulky disease (≥ 7.5 cm) and extralymphatic disease. This arm was compared with RICOVER noRT arm. The findings were that in a per-protocol analysis, RT for bulky (≥7.5 cm) improved HR for EFS, PFS, and OS. This was not the case when all eligible patients were included (including the 11 patients that did not get RT per trial design). Thus, answers A, B, and D are incorrect.

240. At what testicular dose is surveillance for testosterone deficiency recommended for childhood and young adult survivors of cancer?
   a. 1 Gy
   b. 3 Gy
   c. 6 Gy
   d. 12 Gy

Key: D
Rationale: 1 – 3 Gy exposure is associated with possibly reversible azoospermia; 3 – 6 Gy is associated with possibly but unlikely reversible azoospermia; > 6 Gy, azoospermia is probably permanent; > 12 Gy is associated with increased risk of testosterone deficiency.

241. What is the MOST common mutation in pediatric gliomas?
   a. H3.3
   b. IDH1
   c. MYCN
   d. PTCH1

Key: A
Rationale: Histone H3.3 mutations are the most common mutation in pediatric gliomas. IDH1 mutations occur rarely, typically in adolescents or young adults. MYCN amplification and PTCH1 mutation occur in medulloblastoma.

242. What percentage of breast cancer is related to BRCA1 mutation?
   a. 5%
   b. 10%
   c. 25%
   d. 50%

Key: A
Rationale: Mutations in BRCA1 are found in 5% of all breast cancer cases. They are also associated with ovarian and prostate cancer. BRCA1 mutations are rarely found in sporadic breast cancer.
243. In error propagation governed by the normal distribution, if the measurements of x and y are independent and subject only to random uncertainties, then the uncertainty dq in the calculated value of q = x + y is:
   a. linearly
   b. exponentially
   c. quadratically
   d. nonparametrically

**Key:** NOTE: This item was 0-weighted for scoring purposes upon post-exam statistical item analysis (did not count for or against candidate in calculation of test scores).

**Rationale:** The sum in quadrature of the independent and random uncertainties is the propagation of error by the normal distribution.

**References:** Taylor, John R. An Introduction to Error Analysis. 1997, p. 58.

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244. When mastectomy is performed for treatment of DCIS, what is the approximate rate of occult multicentric disease?
   a. 10 to 15%
   b. 20 to 30%
   c. 35 to 40%
   d. >50%

**Key:** B

**Rationale:** Multicentric DCIS is an indication for mastectomy. The approximate rate of occult multicentric disease is 20 to 30%. Occult invasive disease of approximately 10% is also found in mastectomy specimens removed for diagnosis of DCIS.


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245. To ensure coverage of the thecal sac during CSI, the inferior border is BEST placed at approximately:
   a. L3
   b. L5
   c. S3
   d. Coccyx

**Key:** C

**Rationale:** For an individual patient, the thecal sac is best determined by the sagittal T2 MRI. At a population level, the mean position is at approximately S2. For coverage with a margin, the most appropriate level to cover is approximately S3. L3 is below the inferior extent of the spinal cord (not the thecal sac).


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246. For a polyenergetic photon beam, how does the first half value layer (HVL) compare to the second HVL?
   a. Larger
   b. Smaller
   c. Equal
   d. Change depends on beam energy

**Key:** B

**Rationale:** In polyenergetic beams, the first half value layer is smaller than the second as the first HVL removes the less energetic components of the beam preferentially. Because of this, the 2nd HVL will attenuate higher energy photons and will thus need to be thicker.

247. What is the mechanism of action of Denosumab?
   a. Blocks the synthesis of adrenal androgens
   b. Complexes with bone mineral hydroxyapatite
   c. Acts as autologous active cellular immunotherapy
   d. An anti-RANKL antibody

**Key:** D

**Rationale:** Denosumab is an antibody that binds to and inhibits RANKL, a molecule that normally functions to activate Osteoclasts, thereby protecting bone from degradation. The other choices describe the mechanisms of other agents demonstrating a survival benefit in mCRPC. Abiraterone acetate inhibits cytochrome P450 17 (CYP17) α-hydroxylase and cytochrome17,20 (C17,20)-lyase, which are enzymes critical for androgen synthesis found in the adrenal glands. Radium Ra-223 dichloride complexes with bone mineral hydroxyapatite and delivers alpha particle radiation to sites of bone metastasis. Lastly, Sipuleucel-T has shown a survival benefit in asymptomatic mCRPC patients, whose mechanism of action is that it acts as autologous active cellular immunity.


248. The T10 dermatome innervates what approximate area?
   a. Nipple line
   b. Xiphoid
   c. Umbilicus
   d. Inguinal crease

**Key:** C

**Rationale:** Dermatomes: T4-Nipple, T10-Umbilicus, L1-Inguinal Crease. The xiphoid is in the same axial plane as approximately T10 vertebral body (not the T10 dermatome).

**References:** Hansen, Netters Clinical Anatomy, 2014.

249. What is the MOST appropriate craniospinal dose for a 7 year old girl with a classic medulloblastoma that has been gross totally resected with malignant cells present in a pre-operative lumbar puncture and no metastases in the brain or spine on MRI?
   a. 18 Gy
   b. 23.4 Gy
   c. 36 Gy
   d. 39.6 Gy

**Key:** C

**Rationale:** This patient has M1 disease and requires high risk treatment regardless of extent of disease or whether her tumor has diffuse anaplasia. High risk therapy includes 36 Gy of craniospinal irradiation. Average risk therapy (what would be indicated if her LP were negative) would call for 23.4 Gy of radiation. 18 Gy has recently been studied on ACNS0331 for average risk patients and was reported at ASTRO 2016 as being inferior to 23.4 Gy of craniospinal irradiation. 39.6 Gy of spinal irradiation is sometimes employed when patients have diffuse leptomeningeal disease of the spine.

Which mechanism of cell death is characterized by a loss in cell size, chromatin condensation, enzymatic fragmentation of DNA and overall cellular fragmentation into membrane bound vesicles?

a. Necrosis  
b. Apoptosis  
c. Senescence  
d. Autophagy

Key: B  
Rationale: The changes listed in the question are all indicators of apoptosis. This cell death mechanism is a carefully orchestrated series of steps designed to eliminate and destroy cells while avoiding the release of cellular constituents into the surrounding medium thus preventing an inflammatory immune response. The resulting membrane bound vesicles are easily phagocytized by neighboring cells. Necrosis is just the opposite and leads to burst cells with incipient inflammation. Senescence does not actually kill the cell in a physiological sense but renders it incapable of further division. Autophagy devours organelles within the cell usually as a mechanism to conserve resources in stressed or starving cells. It is unclear whether autophagy is a death mechanism in and of itself or whether it is an intermediate step in some other death process.  

Which pediatric GTV is defined by the post-chemotherapy, pre-surgical extent of disease?

a. Neuroblastoma  
b. Rhabdomyosarcoma  
c. Wilms tumor  
d. Ewing’s sarcoma

Key: A  
Rationale: For neuroblastoma, the target volume is defined by the post-induction chemotherapy, pre-surgical volume of tumor. For rhabdomyosarcoma, tumor volumes treated to 50.4 Gy with significant response to chemotherapy can be reduced after 30.6 Gy. For Wilms tumor, volumes are classic flank, whole abdomen, or whole lung. For Ewing’s sarcoma, the tumor present before chemotherapy or surgery is included.  

What was observed in the MegaMouse project concerning heritable effects of radiation?

a. Temporary sterility in males seen > 6 Gy  
b. Males were more radioresistant than females  
c. Genetic effects increased with more time between exposure and conception  
d. Mutations increased linearly with dose and dose rate

Key: D  
Rationale: Mutations increase linearly with dose and dose rate. Males were more radiosensitive than females. Temporary sterility in males was seen with doses significantly less than 1 Gy. The longer the period between radiation exposure and conception, the less the genetic effects on the offspring.  
**253.** Relative to a single dose exposure, how is the RBE of neutrons affected by fractionation in comparison to RBE of fractionated photons?
   a. Decreases marginally
   b. Decreases significantly
   c. Increases but to lesser extent
   d. Increases by the same extent

**Key:** NOTE: This item was multi-keyed for scoring purposes upon post-exam statistical item analysis (Both A and C were given credit as correct responses).

**Rationale:** The RBE of high LET radiation increases with fractionation, because the shoulder region is low after single or fractionated exposures from high LET, indicating little sparing. The alpha component of cell kill dominates, and death more an exponential component of dose. After exposure to x-rays, the shoulder region of the survival curve remains after each fraction and is higher than after exposure to neutrons, and thus the ability to repair sublethal damage is higher. This results in higher RBE for neutrons after fractionated exposures. The RBE would not decrease with fractionation, even if the LET of the high LET radiation was 100keV/μm – in fact one would expect RBE to be highest for neutrons at that LET.

**References:** Hall and Giaccia, Radiobiology for the Radiologist, Sixth ed, p. 70, 71, and 109.

**254.** For a proliferating population of tumor cells, how would the clonogenic survival change when the time interval between two X-rays fractions is increased from 30 minutes to 4 hours?
   a. Increase
   b. Decrease
   c. No change
   d. Cannot be determined

**Key:** A

**Rationale:** The repair time for mammalian cells in culture is typically 1-2 hours. Increasing fraction time from 30 minutes to 2 hours would increase surviving fraction in culture, especially if the cells are non-proliferative as there would not likely be a decrease due to reassortment. Cells can repair sublethal damage with normal p53 function. Stable dose rate would not have an effect. Non-proliferative cells are not in the sensitive M phase of the cell cycle, which would indicate that they are dividing.

**References:** Hall and Giaccia, Radiobiology for the Radiologist, Chapter 5, Sixth ed.

**255.** Regarding the Phase III non-inferiority trial for follicular lymphoma (FORT), how did 4 Gy compare to 24 Gy?
   a. Better time to progression
   b. Equivalent time to progression
   c. Worse time to progression
   d. Improved OS

**Key:** C

**Rationale:** FORT is a prospective randomized, unblinded phase 3 non-inferiority study comparing 4 Gy vs 24 Gy for follicular lymphoma or marginal zone lymphoma. Time to local progression in the 4 Gy was not non-inferior to 24 Gy. The HR was 3.42 (95% CI 2.09-5.55 p<0.0001), showing the 4 Gy was actually worse (see figure 2A in the study). Toxicity was low in both arms. Lowest was in the 4 Gy arm, as would be expected.

**References:** Hoskin PJ. Lancet Oncology, 15(4); 2014, 457-63.
256. How far within the light field should the patient be positioned in order to receive full dose for a TBI treatment?
   a. Touching the edges of the light field at treatment distance
   b. Touching the edges of the light field at LINAC isocenter
   c. More than the size of the penumbra at treatment distance
   d. Less than the size of the penumbra at LINAC isocenter

Key: C
Rationale: The patient should be at a distance at least the size of the penumbra from the edge of the light field at the treatment distance. At a large distance such as used in TBI, the penumbra will increase with distance, which should be taken into account.


257. Approximately what percentage of patients on the MA-20 and EORTC 22922 trials of regional nodal irradiation in early stage breast cancer were treated with mastectomy?
   a. 0% on either
   b. 0% on MA20 and 25% on EORTC
   c. 25% on MA20 and 0% on EORTC
   d. 25% on either

Key: B
Rationale: On the MA-20 trial, all patients were treated with breast conserving surgery. 24% of patients on the EORTC trial had mastectomy. No neoadjuvant chemotherapy was used. Patient eligibility for MA-20 included: invasive breast carcinoma with breast-conserving surgery and SLNBx or AxLND with positive axillary lymph nodes or negative axillary nodes with high-risk features. (High risk features defined as primary tumor measuring 5 cm or more or 2 cm or more with fewer than 10 axillary nodes removed and at least one of the following: grade 3, ER negative, or LVSI). AxLND was required for patients with positive results on SLNBx.
Eligibility criteria for the EORTC trial included: unilateral stage I, II, or III breast cancer with either centrally or medially located primary tumor, irrespective of axillary involvement, or an externally located tumor with axillary involvement. Eligible patients had undergone mastectomy or breast-conserving surgery and AxLND. SLNBx was later allowed however AxLND was required if SLNBx was positive.


258. The MOST important quality assurance test of a LINAC kilovoltage (kV) cone beam CT (CBCT) system used for IGRT is:
   a. image soft tissue contrast.
   b. coincidence between the MV and kV imaging isocenters.
   c. Hounsfield unit value and constancy.
   d. spatial resolution.

Key: B
Rationale: If the MV and kV isocenters are not coincident the patient may be positioned incorrectly without this being apparent. Choice D is a correct statement by itself but it does not apply to kV CBCT. Choice A and C relate to image quality. These are important but not as important as choice B.

259. Compared to plaque brachytherapy, what is an advantage of proton therapy for the treatment of uveal melanoma?
   a. Less expensive
   b. Treats larger tumors
   c. Mobile radiation field
   d. Lower risk of enucleation

Key: B
Rationale: Proton therapy for treatment of uveal melanoma is more expensive than brachytherapy. Plaque brachytherapy provides a mobile radiation field that moves with the eye; proton therapy is a static treatment. On a meta-analysis of outcomes, there was no difference in the risk of enucleation between charged-particle therapy and brachytherapy. Proton therapy allows for the treatment of larger tumors, including tumors that touch the optic disc.


260. Which protein set is associated with stress (radiation)-induced premature cellular senescence?
   a. p16, pRB
   b. BAX, PUMA, APAF1
   c. hAPG12, MAP1LC3
   d. RIPK1, MLKL

Key: A
Rationale: The proteins p16 (Cyclin-dependent kinase inhibitor 2A) and pRB (Retinoblastoma protein) form a pathway that blocks transcription factors of the E2F family thus preventing cells from leaving G1 and moving into the S phase of the cell cycle. Under certain conditions this cell cycle arrest can be permanent leading to stress induced premature senescence. BAX PUMA and APAF1 code proteins associated with apoptosis while HAPG12 and MAP1LC3 are linked to autophagy. RIPK1 and MLKL code for proteins involved with “Necrosis” a regulated form of necrosis.


261. What histologic or molecular finding is most consistent with a pilocytic astrocytoma?
   a. Rosenthal fibers
   b. Palisading necrosis
   c. Translocation of chromosomes 11 and 22
   d. Loss of heterozygosity of 1p and 16q

Key: A
Rationale: This is a characteristic histologic finding of pilocytic astrocytomas. Translation of chromosomes 11 and 22, palisading necrosis, Loss of heterozygosity of 1p and 16q, N-Myc amplification are associated with Ewing Sarcoma, glioblastoma, poor prognosis in Wilms Tumor, and poor prognosis in Neuroblastoma.

262. According to Task Group 142 of the AAPM, what is the recommended tolerance for monthly dosimetric output constancy?
   a. 1%
   b. 2%
   c. 3%
   d. 5%

   **Key:** B
   **Rationale:** TG-142 recommends that monthly output constancy should be within 2% of its baseline value. This is a relative measure, and the baseline is typically obtained from the most recent annual quality assurance testing. TG-142 recommends a daily constancy tolerance within 3%, and annual output calibration should be accurate to within 1% of the absolute output (dose per monitor unit to water) value. These recommendations are made to recognize the varying levels of accuracy achievable for typical tests in each frequency category.

263. A pair of anterior oblique beams normal (90°) to each other are used to treat a lesion in the sternum. What is the optimum wedge angle to ensure homogeneity across the lesion?
   a. 15°
   b. 30°
   c. 45°
   d. 60°

   **Key:** C
   **Rationale:** Wedge angle=90°-hinge angle/2. Therefore, the wedge angle will be 45 degrees.

264. Both the RTOG 9501 and EORTC 22931 trials showed that the addition of cisplatin to adjuvant radiation therapy resulted in a statistically significant improvement in which of the following?
   a. Local-regional failure
   b. Distant metastases
   c. Overall survival
   d. Grade 3 toxicity

   **Key:** A
   **Rationale:** The RTOG 9501 and EORTC 22931 trials compared adjuvant radiation with and without concurrent chemotherapy in patients at high risk of recurrence. Both studies showed a significant improvement in local-regional failure and increase in grade 3 or higher toxicity. Neither trial showed a significant improvement in distant metastases and only the EORTC 22931 trial showed a statistically significant improvement in overall survival. Retrospective subgroup analysis of combined data from these 2 studies established the guidelines currently used to determine adjuvant treatment (as in question 126).
265. Which lymph nodes are included in a D1 dissection for gastric cancer?
   a. Infrapyloric
   b. Celiac
   c. Common hepatic
   d. Retropancreatic

   **Key:** A
   **Rationale:** D1 lymph nodes include the perigastric lymph nodes including the R/L paracardial LN, the greater/lesser curvature LN, and the supra and infra-pyloric LNs.

266. What was the radiation treatment arm in the UK NCRI RAPID trial of early stage Hodgkin lymphoma patients with negative PET after 3 cycles of ABVD?
   a. IFRT 30 Gy
   b. IFRT 20 Gy
   c. ISRT 30 Gy
   d. ISRT 20 Gy

   **Key:** A
   **Rationale:** The UK NCRI RAPID trial was a noninferiority trial for stage IA and IIA Hodgkin lymphoma patients who received 3 cycles of ABVD. Those who had a negative interval PET scan (defined as Deauville score 1 or 2) were randomized to 30 Gy using involved field radiation therapy versus observation.

267. A patient presents with cervical lymphadenopathy positive for SCC on FNA. Exam and laryngoscopy do not indicate a primary site of disease. Which test best correlates with identification of the primary on EUA?
   a. PET/CT
   b. EGFR staining
   c. MRI
   d. p16 staining

   **Key:** D
   **Rationale:** Patients with p16 positive disease were much more likely to have the primary identified on EUA and biopsies. Imaging was much less likely to indicate which patients would have an identifiable primary. Sensitivity of identifying the primary site with p16 status is 85.7% vs only 42.9% with PET/CT. The accuracy is 83.3% vs 68.5%, respectively. For p16 positive patients the most common primary site identified was the tonsil.

268. The combination of low-energy neutrons with Boron Neutron-Capture Therapy using BSH (10B enriched sodium borocaptate, Na2B12H11SH) causes tumor cell killing by the production of:
   a. high-LET protons.
   b. low-LET protons.
   c. both high-LET protons and low-LET carbon ions.
   d. high-LET alpha particles and 7Li ions.

   **Key:** D
   **Rationale:** The production of alpha particles and 7Li occurs when a drug containing boron (such as BSH) is irradiated with low energy neutrons during boron neutron capture therapy
   **References:** Hall and Giaccia, Radiobiology for the Radiologist, Sixth ed., p. 409.
269. Which is attracted by MRN (Mre11-Rad50-Nbs1) during recognition of a DNA double strand break? 
   a. Chk2
   b. BRCA1
   c. ATM
   d. H2AX

**Key:** C  
**Rationale:** ATM, which initiates mutual phosphorylation with Chk2 and a phosphorylation cascade of many downstream targets to initiate DNA repair. Can cause change in cell cycle and chromatin.  
**References:** Uziel, et.al. Requirement of the MRN complex for ATM activation by DNA damage. EMBO J 2003; 22(20):5612-5621.

270. How many image values can be encoded in a 12-bit grayscale image?  
   a. 144 
   b. 256 
   c. 1728 
   d. 4096 

**Key:** D  
**Rationale:** A 12-bit data element contains $2^{12} = 4096$ possible values. In a grayscale image, each value represents one greyscale level. This is the typical bit depth of a CT image. 

271. According to RTOG 9802, which patient with gross total resection of a low grade glioma would benefit from the addition of chemotherapy after radiation?  
   a. 48 year old woman 
   b. 37 year old man 
   c. 26 year old woman 
   d. 19 year old man 

**Key:** A  
**Rationale:** RTOG 9802 randomized high risk low grade glioma patients, defined as either >40 years after biopsy/resection or patients age 18 – 39 years after subtotal resection, to either radiation versus radiation followed by PCV. The updated analysis found both a progression free survival benefit and overall survival benefit.  

272. What were the two arms of the randomized trial EORTC 24891 which evaluated larynx preservation for hypopharyngeal squamous cell carcinoma?  
   a. Total laryngectomy + RT vs. induction chemo + RT for complete responders  
   b. Total laryngectomy + RT vs. concurrent chemoRT  
   c. Induction chemo + RT vs. concurrent chemoRT  
   d. Induction chemo + RT vs. RT alone 

**Key:** A  
**Rationale:** The two arms of EORTC 24891 were total laryngectomy followed by RT versus a larynx preservation approach with induction cisplatin/5-FU x 3 cycles followed by RT in complete responders. Patients who did not achieve a complete response proceeded to total laryngectomy and adjuvant therapy as indicated. The endpoints were OS, PFS and survival with a functional larynx. OS and PFS were similar in both arms. Survival with a functional larynx was 8.7% at 10 years.  
273. In what order do cytopenias appear after 4-6 Gy TBI?
   a. Lymphopenia, granulocytopenia, thrombocytopenia, anemia
   b. Lymphopenia, thrombocytopenia, granulocytopenia, anemia
   c. Thrombocytopenia, lymphopenia, granulocytopenia, anemia
   d. Thrombocytopenia, granulocytopenia, lymphopenia, anemia

Key: A
Rationale: Lymphocytes are very radiosensitive and doses as low as 0.3 Gy can reduce the number of lymphocytes. After 4-5 Gy TBI the number of lymphocytes rapidly decreases, and this is followed by a decrease in the number of granulocytes. Higher doses are needed to reduce the granulocyte number, and this typically takes a week because of the mobilization of the reserve pool.

274. For esophageal cancers, long-term toxicity to which organ at risk can be reduced with the use of IMRT?
   a. Lung
   b. Spinal Cord
   c. Stomach
   d. Heart

Key: D
Rationale: In Lin et al, MRT was not found to be associated with EC-specific mortality (hazard ratio [HR], 0.93; 95% confidence interval [95% CI], 0.80-1.10) or pulmonary mortality (HR, 1.11; 95% CI, 0.37-3.36), but was significantly associated with lower all-cause mortality (HR, 0.83; 95% CI, 0.72-0.95), cardiac mortality (HR, 0.18; 95% CI, 0.06-0.54), and other-cause mortality (HR, 0.54; 95% CI, 0.35-0.84). In Cole et al, treatment of patients with distal oesophageal cancer using IMRT significantly decreases the exposure of the heart and right coronary artery when compared with 3D-CRT.

275. Positive staining for p16 in tonsil SCC correlates with:
   a. EBV infection.
   b. a favorable response to therapy.
   c. high EGFR expression.
   d. a decreased rate of nodal metastases.

Key: B
Rationale: p16 is the strongest independent prognostic marker in oropharynx SCC and correlates with HPV associated disease. p16 staining is negatively correlated with EGFR expression. EBV depresses p16 expression. p16 positive tumors are more likely to have regional nodal metastases.
Rüveyda et al., Dual role for p16 in the metastasis process of HPV positive head and neck cancers, Mol Cancer, PMCID: PMC5492443, 16, 2017, 113.

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276. In a combined review of locoregional recurrence risk following neoadjuvant chemotherapy for patients treated on NSABP B-18 or B-27:
   a. the risk of nodal failure was < 5% in patients achieving a pCR in the nodes who then underwent BCS followed by breast irradiation alone.
   b. use of post mastectomy radiation was at the discretion of the treating physician.
   c. age (< 50 vs. > 50) was a significant independent predictor of LRR for patients undergoing mastectomy.
   d. the 10-year LRR risk was < 10% for patients undergoing either BCS or mastectomy.

   **Key:** A
   **Rationale:** A: Nodal recurrence in patients who achieved clearance of the LNs with neoadjuvant chemotherapy ranges from 0-2.4% depending on the subgroup analysed.
   B: Patients undergoing mastectomy did not receive adjuvant radiation.
   C: In patients undergoing a mastectomy, age was not an independent predictor of LRR. It was a predictor of LRR for patients undergoing lumpectomy.
   D: LRR risk at 10 years was 12.3% for patients undergoing mastectomy and 10.3% for patients undergoing BCS.
   **References:** Mamounas EP et al, Predictors of LRR after Neoadjuvant Chemotherapy: Results from Combined Analysis of NSABP B-18 and B-27, JCO, Nov 10, 2012; 30(32), 3960.

277. What is the BED of 20 Gy in 5 fractions for late normal tissue reactions?
   a. 6 Gy
   b. 36 Gy
   c. 46 Gy
   d. 56 Gy

   **Key:** C
   **Rationale:** The biologically effective dose (BED)= nd x (1+d/α/β), where n is the number of fractions and d is the dose per fraction. The α/β ratio for late responding normal tissue is 3 Gy. 5 Fx in 20 Gy = BED (5.4)x(1+d/3) = 46.6 Gy.
   **References:** Hall and Giaccia. Radiobiology for the Radiologist. Chapter 3: Cell survival curves. 6th ed.

278. Which is the MOST common type of DNA damage caused by 1 Gy of low LET ionizing radiation?
   a. Double strand breaks
   b. Single strand breaks
   c. Complex clustered damage
   d. Base damage

   **Key:** D
   **Rationale:** Typically there are 1000-2500 base damages, 40 double strand breaks, 1000 single strand breaks and 800-1600 sugar damages per Gray of low LET radiation
279. What are the key regulators of G1/S cell cycle transition process in the mammalian cell cycle?
   a. E2F/pRb
   b. Cyclin B/CKD1
   c. p27/p16
   d. Rad50/Mre11

Key: A
Rationale: Phosphorylation of Rb by cyclin D/CDK4 (pRb) triggers G1/S transition. At a critical level of phosphorylation, E2F is released from pRb. This activates the transcription of Cyclin E which complexes with Cdk2 to fully release pRb repression by further phosphorylation, establishing a positive feedback loop. Cyclin B/CKD1 is involved in G2 transition, p27/p16 are anti-mitogens involved in the induction of radiation induced cell cycle arrest. Rad50/Mre11 are involved in the recognition of radiation induced DNA double strand breaks.

280. The primary factor contributing to skin dose for LINAC megavoltage photon beams is:
   a. low energy photons in the beam.
   b. photons scattered in the head of the LINAC.
   c. the use of multileaf collimators (MLCs).
   d. electron contamination of the beam.

Key: D
Rationale: The primary contributor to skin dose is electron contamination of the beam. Beam modifiers usually contribute more electron contamination than they remove.

281. RTOG 0529 demonstrated that hematological toxicity was significantly reduced compared to RTOG 9811. What was the dose constraint used for the iliac crests?
   a. No more than 90% above 10 Gy
   b. No more than 75% above 20 Gy
   c. No more than 50% above 30 Gy
   d. No more than 25% above 40 Gy

Key: NOTE: This item was 0-weighted for scoring purposes upon post-exam statistical item analysis (did not count for or against candidate in calculation of test scores).
Rationale: In table 1, the iliac crest tolerances are detailed: no more than 50% above 30 Gy, no more then 35% above 40 Gy, and no more than 5% above 44 Gy.

282. How would D0 values of a radiation survival curve change with increasing oxygenation?
   a. Decrease
   b. Increase
   c. No change
   d. Increase then decrease

Key: A
Rationale: The alpha component of cell kill in this scenario is likely higher than the beta. A survival curve exhibiting a D0 of .1 Gy would indicate that little repair would be present, and cell death is exponential function of dose. If cells have non-hydroxylated HIF a, then the cells are under hypoxic stress hypoxic environment. High LET radiation has a low OER, and if the D0 is 0.1, this would indicate must be high LET; little sparing occurs for high LET radiation in hypoxic environment. The alpha component of cell kill would also therefore be high. If low LET radiation was used, the D0 in a hypoxic environment would be higher. Increasing dose rate of high LET in a hypoxic environment would not substantially lower D0.
References: Hall and Giaccia, Radiobiology for the Radiologist, Sixth ed, p. 87 and 101.
283. What is the mechanism of action of pazopanib?
   a. Multi-kinase inhibitor targeting a number of receptor tyrosine kinases
   b. Inhibitor of the mammalian target of Ramaycin (mTOR) protein
   c. Antibody that binds and blocks the programmed cell death protein 1 (PD-1)
   d. Monoclonal antibody directed against the epidermal growth factor receptor

Key: A
Rationale: Pazopanib is a selective multi-targeted receptor tyrosine kinase inhibitor. Temsirolimus is an inhibitor of the mammalian target of Ramaycin (mTOR) protein. Pembrolizumab is a checkpoint inhibitor that binds and blocks the programmed cell death protein 1 (PD-1) located on lymphocytes. Cetuximab is a monoclonal antibody directed against the epidermal growth factor receptor.


284. What is the approximate α/β ratio for prostate cancer?
   a. 1.5
   b. 4.5
   c. 7.5
   d. 10

Key: A
Rationale: Prostate cancer has been shown to have low α/β ratio of 1.5

285. When using IMRT to treat vulvar cancer, the CTV caudal extent of the inguinofemoral nodal basin is defined by the:
   a. superior pubic ramus
   b. lateral to the rectus femoris muscle
   c. medial border of the sartorius muscle
   d. top of the lesser trochanter of the femur

Key: D
Rationale: Symmetrical geometric expansion on the vessels should NOT be used for the inguinofemoral nodes. The inguinofemoral nodal CTV should extend laterally from the inguinofemoral vessels to the medial border of the sartorius and rectus femoris muscles, posteriorly to the anterior rectus medialis muscle and medially to the pectineus muscle or 2.5-3 cm medially from the vessels. Anteriorally the volume should extend to the anterior border of the sartorius muscle. The caudal extent of the nodal basin is the top of the lesser trochanter of the femur.

References: NCCN, 1.2017

286. How does ICRU define LDR brachytherapy (Gy/hr)?
   a. 0.4 to 2
   b. 4 to 6
   c. 8 to 10
   d. >12

Key: A
Rationale: LDR is 0.4-2 Gy/hr; MDR is 2-12 Gy/hr; HDR > 12 Gy/hr.
References: ICRU
287. What are the target volumes for adjuvant radiation therapy after a total parotidectomy and ipsilateral neck dissection for a node-positive high-grade salivary ductal carcinoma?
   a. Tumor bed-alone
   b. Ipsilateral neck
   c. Tumor bed and ipsilateral neck
   d. Tumor bed and bilateral neck

Key: C
Rationale: Adjuvant radiation therapy for high-grade salivary gland tumors includes the parotid bed and the ipsilateral neck.
References: Gunderson and Tepper, Clinical Radiation Oncology, 2015, Elsevier, 4th, 698-714.

288. What is the “power” of a test or study?
   a. The accuracy to which the true mean of a distribution can be known
   b. The precision to which the mean of a distribution can be known
   c. The confidence level selected to compare two data sets
   d. The ability to detect a true difference

Key: D
Rationale: The power of a test is the probability of detecting a difference that exists. It can be stated as the probability of rejecting the null hypothesis when it is indeed false or, equivalently, concluding that the alternative hypothesis is true when it really is true. It is intimately related to the sample size used in the study.

289. Which of the following biological tumor characteristic contributes to improved tumor control with conventional fractionation?
   a. Low SF2
   b. Short Tpot
   c. High number of stem cells
   d. No reoxygenation

Key: A
Rationale: A large number of tumor clonogens would be deleterious to tumor control and would require a higher total dose for tumor eradication. A low SF2 indicates radiosensitivity and would suggest that the fraction of tumor cells that survive treatment with a 2 Gy fraction is low. A long Tpot induces a slowly proliferating tumor would this aid in tumor control as it indicated a low potential for significant repopulation during a course of radiation. Rapid reoxygenation may improve the efficacy of radiation killing by oxygenating any potentially radioresistance hypoxic cells.

290. In the phase III randomized study (CREST) evaluating the addition of 30 Gy of consolidative chest RT to chemotherapy and PCI for extensive stage SCLC:
   a. the primary endpoint of improved OS at 1 year was met.
   b. PCI had greater survival impact than the chest radiation.
   c. a doubling of grade 3-4 toxicities was observed.
   d. a 10% improvement in 2-yr OS was seen.

Key: D
Rationale: Slotman et al. study of ES-SCLC patients with any response of RCT of PCI alone vs. PCI and thoracic RT showed a non-significant difference in the primary end-point of 1 year OS (28% vs. 33%, p=0.066). On secondary analysis, a statistically significant 2-year OS improvement was noted (3% vs. 13%, p=0.004). Grade 3 or higher toxic effects occurred in 26 patients in the thoracic radiotherapy group and 18 patients in the control group (p=0.28) All patients received PCI, so this was not tested, but historical data suggests a survival benefit of ~5% for PCI, less than the observed 10% benefit to chest RT in this study.
291. Regarding cell survival, sublethal damage repair is:
   a. described by the \( \beta \) component of LQ model.
   b. enhanced by high temperatures.
   c. similar after high LET or low LET radiation.
   d. complete 15 minutes after irradiation.

   **Key:** A

   **Rationale:** The shoulder region of the cell survival curve represents sublethal damage repair, and that is related to the beta component of cell kill. High temperatures over 40°C would enhance cell kill, as would exposing cells to high LET radiations vs low. SLDR is generally complete by 1-2 hours.

   **References:** Hall and Giaccia, Radiobiology for the Radiologist, Sixth ed, p. 70.

292. What statistical method measures the degree of reliability between different and independent radiologists?
   a. McNemar’s test
   b. Chi-square test
   c. One-way ANOVA
   d. Kappa coefficient

   **Key:** D

   **Rationale:** The Kappa coefficient is a widely used statistic for measuring the degree of reliability between different and independent raters. It compares the agreement against that which might be expected by chance. The Kappa coefficient ranges from 1 (perfect agreement) to -1 (complete disagreement). Here is one possible interpretation of Kappa.

   - Poor agreement = Less than 0.20
   - Fair agreement = 0.20 to 0.40
   - Moderate agreement = 0.40 to 0.60
   - Good agreement = 0.60 to 0.80
   - Very good agreement = 0.80 to 1.00


293. What is the total recommended dose (EBRT + LDR equivalent brachytherapy) for a vaginal cuff recurrence following hysterectomy and observation for endometrial cancer?
   a. 45 – 50 Gy
   b. 55 – 60 Gy
   c. 75 – 80 Gy
   d. 85 – 90 Gy

   **Key:** C

   **Rationale:** Retrospective studies suggest a dose-response relationship for recurrent vaginal tumors. Other choices are too high or too low.


294. Which photoelectron interactions dominate when the mass attenuation coefficient of an x-ray beam in water is similar to that of lead?
   a. Coherent
   b. Photoelectric
   c. Pair
   d. Compton

   **Key:** D

   **Rationale:** In the Compton range of energies, the total mass attenuation coefficient of lead and water do not differ greatly since this type of interaction is independent of atomic number.

   **References:** Khan. The Physics of Radiation Therapy. Lippincott Williams and Wilkins. 2003. 3rd Ed.
295. When patient specific IMRT QA is performed, which criteria are evaluated when gamma analysis is applied to the planned and measured dose distributions?
   a. Absolute dose agreement and absolute distance to agreement
   b. Absolute dose agreement and relative distance to agreement
   c. Relative dose agreement and absolute distance to agreement
   d. Relative dose agreement and relative distance to agreement

**Key:** C

**Rationale:** Gamma is a composite metric to evaluate the similarity of two dose distributions. Most often this analysis is performed between spatially aligned planned and measured dose distributions in order to verify accurate delivery of an IMRT plan. The difference between the measured and planned doses is evaluated against a relative value (say, 3% of the measured dose) because it allows variability depending on the location in the dose distribution. An absolute value risks being either too stringent in high dose regions or too accepting in low dose regions. Distance to agreement between the measured and planned doses is evaluated with an absolute value (say, 3 mm) because spatial uncertainty is not a function of position. The absolute distance to agreement value allows for small spatial uncertainties to exist in experimental setup and delivery without causing failure of the calculation in high gradient regions where dose changes quickly as a function of location.


296. Regarding GEC-ESTRO (IV) recommendations for MRI based brachytherapy for cervical cancer, which images provide the gold standard for visualization of tumor and critical organs?
   a. T1 with pelvic surface coil
   b. T2 with pelvic surface coil
   c. T1 without pelvic surface coil
   d. T2 without pelvic surface coil

**Key:** B

**Rationale:** It is useful to perform pelvic MRI scanning prior to radiotherapy ("Pre-RT-MRI examination") and at the time of BT ("BT MRI examination") with one MR imager. Both low and high-field imagers, as well as both open and close magnet configurations conform to the requirements of 3D image-based cervical cancer BT. Multiplanar (transversal, sagittal, coronal and oblique image orientation) T2-weighted images obtained with pelvic surface coils are considered as the golden standard for visualisation of the tumour and the critical organs. The use of complementary MRI sequences (e.g. contrast-enhanced T1-weighted or 3D isotropic MRI sequences) is optional. Patient preparation has to be adapted to the needs of BT intervention and MR imaging. It is recommended to visualise and interpret the MR images on dedicated DICOM-viewer workstations, which should also assist the contouring procedure.

**References:** Dimopoulos, Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (IV): Basic principles and parameters for MRI imaging within the frame of image based adaptive cervix cancer brachytherapy, Radiotherapy and Oncology, 2012, 103, 113-122.

297. The required transmission factor, B, for a primary radiation barrier increases with the increase of which factor?
   a. Workload
   b. Use factor
   c. Occupancy factor
   d. Distance

**Key:** D

**Rationale:** \( B = P \times d^2 / WUT \). Inverse square effect.

298. Which is NOT a contributing factor to the proton beam range uncertainty?
   a. CTV delineation
   b. Tissue heterogeneities
   c. Accelerator energy
   d. Conversion of CT number to linear stopping power

Key: A
Rationale: All of the following except CTV delineation contribute to the uncertainty in the proton range.

299. In the US, inflammatory breast cancer accounts for what proportion of all breast cancers?
   a. <1%
   b. 1-5%
   c. 7-10%
   d. 12-15%

Key: B
Rationale: Inflammatory breast cancer (IBC) accounts for about 2% of all breast cancer cases. Even with trimodality therapy, outcomes are poor and IBC comprised 7% of all breast cancer deaths.

300. Regarding muscle invasive bladder cancer, which chemotherapy regimen, when combined with radiotherapy, has been shown in a randomized phase III trial to improve locoregional control over radiotherapy alone?
   a. 5FU and gemcitabine
   b. Carboplatin and gemcitabine
   c. Fluorouracil and mitomycin C
   d. Carboplatin and mitomycin C

Key: C
Rationale: At 2 years, rates of locoregional disease–free survival were 67% (95% confidence interval [CI], 59 to 74) in the chemoradiotherapy group and 54% (95% CI, 46 to 62) in the radiotherapy group. With a median follow-up of 69.9 months, the hazard ratio in the chemoradiotherapy group was 0.68 (95% CI, 0.48 to 0.96; P=0.03). Five-year rates of overall survival were 48% (95% CI, 40 to 55) in the chemoradiotherapy group and 35% (95% CI, 28 to 43) in the radiotherapy group (hazard ratio, 0.82; 95% CI, 0.63 to 1.09; P=0.16).